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ORIGINAL ARTICLES

APPLICATIONS OF THE PRAGMATIC METHOD TO PSYCHIATRY*

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WHAT difference would it practically make to anyone if this notion rather than that notion were true? If no practical difference whatever can be traced, then the alternatives mean practically the same thing, and all dispute is idle": such is one of the briefest formulations that Professor William James ever made of the pragmatic method. Again, there can be "no difference in abstract truth that doesn't express itself in a difference in concrete fact, and in conduct consequent upon the fact, imposed on somebody."

That the pragmatic method, altogether aside from any philosophic implications, must have very important relations to medicine would nowadays be denied by no man. In fact, the whole attitude of the medical man to medicine would not suffer if it should receive the designation "pragmatic." The very founder of the idea of pragmatism, Charles Peirce, used to speak of it as the "laboratory habit of mind." Pragmatism in medicine must have especially close relations with treatment and prognosis. This can be clearly seen from one of the better and longer statements of the nature of pragmatism as given by James in Baldwin's *Dictionary of Philosophy and Psychology*: Pragmatism is "the doctrine that the whole meaning of a conception expresses itself in practical consequences, consequences either in the shape of conduct to be recommended or in that of experiences to be expected, if the conception be true; which consequences would be different if it were untrue, and must be different from the consequences by which the meaning of other conceptions is in turn expressed. If a second conception should not appear to have other consequences, then it must really be only the first conception under a different name. In methodology it is certain that to trace and compare their respective consequences is an admirable way of establishing the differing meanings of different conceptions."

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It is my object in the present paper to apply pragmatic principles to some problems of psychiatry.

1. PSYCHIATRY AND CLINICAL NEUROLOGY

In the first place, does psychiatry exist as distinct from neurology? It can be pointed out that the research basis of psychiatry and of clinical neurology is a unit, namely, theoretical neuropathology, considered in both structural and functional aspects. Let us, however, apply the pragmatic method. Is psychiatry only clinical neurology under a different name? The moment we trace and compare the respective consequences of these two ideas, we perceive that clinical neurology leads to a quite different effect upon the patient from that to be expected when psychiatry approaches him. Psychiatrists and clinical neurologists have had no identical education as clinicians, and they have not the same outlook. This is a practical situation which has pragmatic consequences. It is simply a pious wish when we state that clinical neurologists and psychiatrists are all really nothing but neuropsychiatrists. Perhaps they ought to be and perhaps they soon will be, but they are not. It makes a great deal of difference to the patient whether he is approached by a psychiatrist or by a clinical neurologist.

I have elsewhere gone into more detail upon this matter, referring especially to the different points of view, e.g., toward mild cases of schizophrenia (dementia precox) and cyclothymia (manic-depressive psychoses), maintained by neurologist and psychiatrist respectively. I will not here discuss the point further.

Clinical neurology and psychiatry are pragmatic entities, for they have different consequences when their points of view are applied to the victims of disease.

2. THE SO-CALLED "UNITY OF INSANITY"

Turning to the subject matter of psychiatry, the largest question hangs upon whether we define mental diseases as a unit or as a set of entities. English writers, among them some of the more subtle, such as Charles Mercier, have for years plumped for the unitarian view. One must have a certain respect for any Anglo-Saxon view of the topic, seeing that it no doubt has a certain relevance and practical applicability. However, I think the progress of psychiatry proves, not only that mental diseases can be analytically split up into logical entities, but that these logical units have pragmatic value. At the same time that a thinker like Mercier insists upon the "unity of insanity," he also insists upon grades of responsibility in medicolegal cases and claims to be one of the earliest to have made this distinction. In fine, Mercier lugs in at the finish what we practically want in the matter of subdivisions within psychiatry. If we look more narrowly at other British authors, we find that they often dispose of the unity question in mental diseases by throwing into the field of "nervous" diseases everything which does not handily fit a preconceived legal definition of insanity. This again may comport with Anglo-Saxon notions of practicality and may have a certain relevance from the standpoint of law courts. But assuredly we do not get on very measurably in psychiatric research, if we simply redistribute our material to suit some nonmedical criterion, such as some standard of the practical responsibility of mental cases.

It seems to me that the progress of psychopathic hospitals, in the few places in the world where they have been rigorously tried out, shows beyond cavil that psychiatry is an art dealing with numerous entities. Possibly (according to a rough enumeration from popular systematic works) there may be between eighty and one hundred of these practical entities.

The pragmatic question is, what difference does it make to the patient whether he is said to be affiliated with one or the other of these entities? I am not sure that I can prove that there is a different "conduct to be recommended" or different "experience to be expected" (to use James' phrases) for all of these eighty-odd entities. But I am entirely sure that it makes a great difference to the patient whether he is to be placed in one of ten or a dozen major groups of these entities. Perhaps I entirely miss the point of the British contentions for the unity of insanity; but I really can not see that their viewpoint has a leg to stand upon when we contemplate the present nosological situation. It certainly makes a great deal of difference to the patient, as well as to the social unit in which he lives, whether we regard the patient as a victim of neurosyphilis or whether we regard him as a victim of alcoholic psychosis. Now, possibly the English authors would wish to exclude the victim of neurosyphilis and of alcoholic mental disease from the realm of insanity altogether. Very well,—let this happen. We should then at best attain a conception of the unity of insanity only by greatly diminishing its contents, as ordinarily conceived. But would any author deny that it makes a great deal of difference to the patient whether he is a victim of psychoneurosis or of some depression falling in the group termed by Kraepelin manic-depressive psychosis (which I think might as a group better be termed the cyclothymic group)? Now again, if the unitarian wishes to diminish the field of insanity by cutting off the psychoneuroses, so be it. Again we shall attain unity by a Procrustean process. The psychiatrist will give up any insight he may have into the psychoneurotic and hand his patient forthwith over to the clinical neurologist. Yet the research basis for the understanding of psychoneuroses is no doubt identical for both the psychiatrist and the clinical neurologist. Again the pragmatic method should be applied. If it is true that it is going to make a great difference to the patient whether he is regarded psychiatrically or neurologically, then we must decide that there are real differences under discussion.

Parceling out the psychoneuroses and the cyclothymias to the neurologists and the psychiatrists, respectively, may seem logically the right thing to do. Pragmatically I believe it will have, not only practical, but evil consequences if we execute this partition.

3. DIAGNOSIS BY ORDERLY EXCLUSION

Dismissing the question of the unity of insanity, I wish to approach a few other pragmatic questions in psychiatry and to hang them upon the order concept. Last year I advocated before the Association in a paper *"Diagnosis per Exclusionem in Ordine*: General and Psychiatric Remarks" the application of the principle of order in psychiatric diagnosis, and called attention to the existence of eleven major groups of entities which seemed to me to have practical value. Of course I was aware that the principle could be applied to many other branches of

medicine, and I am glad to say that in correspondence with Dr. Richard C. Cabot, we have together concluded that the principle might very effectively be installed at an early date in many of the specialties, if not in the whole of medicine. As Dr. Cabot has said to me, if one gets hold of a *list* of things it is manifest that said list may be turned into a *sequence* or order and that this sequence or order may have practical value. I shall not here repeat the considerations of the above-mentioned paper, at least to any extent; but I wish to claim that the application of the order concept is an example of pragmatic method. It makes a difference to the patient both in "conduct to be recommended" and "experience to be expected" whether we approach him diagnostically in an orderly fashion.

4. NEUROSYPHILIS AND GENERAL PARESIS

It has in the past made a good deal of practical difference to many psychopathic patients that they have not been primarily considered as possibly victims of neurosyphilis. Time was when the Wassermann serum reaction was taken only in cases in which one suspected general paresis. Nowadays so protean have been proved to be the forms of neurosyphilis that for practical purposes no mental patient can fail to be thought possibly syphilitic. That hypothesis must be disposed of one way or the other.

But if neurosyphilitic, what form of neurosyphilis is in play? It makes a great deal of difference to the patient whether we set up the hypothesis that he has general paresis (with all the evil prognostic connotations of that entity) or whether we limit our initial idea to his being merely neurosyphilitic. An application of the pragmatic method to the orderly diagnosis of the subentities of the neurosyphilitic group would make us consider at some point the *nonparetic* forms of neurosyphilis. We should, in the pragmatic interest of the patient, keep our diagnostic ideas in solution at the level of undifferentiated neurosyphilis rather than leap to the diagnosis "general paresis." We have practically seen a great deal of evil happen to patients by reason of these premature leaps to the diagnosis "general paresis," on the basis of a few clinical similarities to the entity as described in books. There is, therefore, much scope for the application of pragmatic method in the field of neurosyphilis.

5. DIAGNOSTIC PRECESSION OF "FOCAL" VERSUS "SYMPTOMATIC" CASES

To facilitate the rest of my discussion I will here reproduce the eleven groups of mental disease from my paper on *"Diagnosis per Exclusionem in Ordine."*

Mental Disease Groups (Orders)

I. Syphilitic	Syphilopsychoses.
II. Feeble-minded	Hypophrenoses.
III. Epileptic	Epileptoses.
IV. Alcoholic, drug, poison	Pharmacopsychoses.
V. Focal brain ("organic," arteriosclerotic)	Encephalopsychoses.
VI. Bodily disease ("symptomatic")	Somatopsychoses.
VII. Senescent, senile	Geriopsychoses.
VIII. Dementia precox, paraphrenic	Schizophrenoses.
IX. Manic-depressive, cyclothymic	Cyclothymoses.
X. Hysteric, psychasthenic, neurasthenic	Psychoneuroses.
XI. Psychopathic, paranoiac, et al	Psychopathoses.

Why is Group V of the Encephalopsychoses placed prior to Group VI, the Somatopsychoses? Logically, it might well seem that we should approach, in the process of diagnosis, the somatic diseases that give rise to mental symptoms prior to the focal brain diseases that produce mental symptoms. But logic is not practice. In the general hospital clinics, where somatic diseases, nonnervous in nature, are habitually approached logically prior to the nervous and mental diseases, we have not found much progress in psychiatry or much grasp of the psychiatric point of view. Mental cases will for many years to come in our hospital practice, devolve more seriously upon the attention of neurologists and psychiatrists than they will upon the attention of internists. If a man has mental disease and if one has excluded the great groups of syphilis, feeble-mindedness, epilepsy, and alcoholism (with all their practical social implications), then one naturally desires to clear up other large brain aspects of this mental case. Although we are in possession of numerous data to show that mental symptoms may be merely symptomatic of bodily (nonneural) diseases, yet there is no doubt that the nervous system exerts in some ways a prior claim on the attention. Perhaps the practical answer would be that in internists' clinics, the order of logical consideration should be reversed and Group VI placed before Group V, whereas in psychiatric clinics the order might remain as stated. Let me insist at this point on something which is logically clear, but practically not always envisaged. *This system of orderly exclusion in diagnosis has nothing whatever to do with the practical order in which data are collected.* It is a plan to be put into effect *after the data are all in hand.* It does not matter whether the data about the pupils or the reflexes are chronologically collected before the data concerning bodily infection. The question is one of logical, not of chronological, priority. In the end, however, I am willing to acknowledge that the question, whether the encephalic or the nonneural somatic conditions should be diagnostically placed in the order I recommend, is an open question. The question can be answered in the long run only pragmatically.

6. DIAGNOSTIC PRECESSION OF SCHIZOPHRENIC VERSUS CYCLOTHYMIC CASES

One other example may be offered looking in the same direction. I have placed the schizophrenoses (dementia precox, etc.,) in Group VIII, ahead of the cyclothymoses (manic-depressive, etc.), Group IX. Now it might be pointed out that as manic depressive phenomena are more nearly normal than schizophrenic phenomena, it should be well to consider the patient normal before we consider him abnormal. Let the patient be regarded as innocent of mental symptoms before he is regarded as guilty of such. Well, the pragmatic answer to this question is that it appears to have important practical consequences whether we consider a patient schizophrenic logically prior to our considering him cyclothymic. A group of schizophrenic symptoms is much more convincing as to a patient's being a victim of the disease schizophrenia than is a group of cyclothymic symptoms convincing as to his being a victim of cyclothymic disease. Just in virtue of the quasi-normality of the ups and downs in mood of the manic-depressive does it transpire that practically every form of mental disease is capable of showing these ups and downs in mood. By consequence

if we fix our minds upon cyclothymic phenomena, we are rather inclined to premature fixation of our minds upon the diagnosis of the entity manic-depressive psychosis. Seeing cyclothymoid symptoms, we rush to the idea of the cyclothymic entity. In short a group of schizophrenic symptoms is much more "pathognomonic" than a group of cyclothymic symptoms. It was upon this pragmatic basis that Group VIII was placed before Group IX.

Why should we place the psychoneuroses in a Group X, following the schizophrenias and cyclothymias? I am bound to admit that this placement was an exceedingly practical one. We have in psychopathic hospital practice seen so many cases in which the diagnosis "nervous prostration" has been affixed to a patient who was really a mild example of schizophrenia or of cyclothymia (and this much to the therapeutic detriment of the cases in question) that it seemed wise to relegate the psychoneuroses to a subsequent position in the diagnostic list for orderly exclusion.

7. PLACEMENT OF INVOLUTION-MELANCHOLIA

Another example of the application of the pragmatic method is in the question of involution-melancholia. Controversy rages as to whether the involution-melancholias belong in the senile group (in my own arrangement, Group VII, the Geriopsychoses) or whether they belong in the cyclothymic (manic-depressive group) Group IX of the above list. Logically there might be some argument for placing the involution-melancholias among the senile and presenile conditions. The very *term* involution suggests this. However, it seems to me that we must grant that we know next to nothing (and pragmatically I should say absolutely nothing) about the etiology and genesis of involution melancholia. No doubt there is a darkling idea that involution melancholia is somehow an endocrine affair. We know nothing about the etiology and genesis of manic-depressive psychoses. But here the pragmatic method allows us to employ even our ignorance to advantage. There is not the slightest doubt that to place a case in the senile or presenile sub-groups of the Geriopsychoses is to give the case an evil prognosis with respect to tissue destruction and degeneration, perhaps unjustly and harmfully.

To place the involution-melancholias in the senile-senescent group is to cause certain experiences to be expected. Now, practically, we know that such experiences are not always to be expected in involution-melancholia, in short that clinical deterioration is not always found to suggest brain tissue degeneration. Pragmatically speaking, therefore, it seems to me that the reply as to the placement of the involution-melancholias is unconditionally to place them in the cyclothymic group, as compared with the senile-senescent group — and this despite our dense ignorance of the nature of involution-melancholia.

SUMMARY

1. Psychiatry should more and more adopt the "Laboratory habit of mind," become more and more pragmatic, and bring itself in line with the rest of medicine.

2. Seven applications of the pragmatic method to psychiatry are offered:

(a) It makes a difference to the patient whether he is seen by a psychiatrist or by a clinical neurologist: There is thus for the moment a real difference between psychiatry and clinical neurology, though the future may destroy that difference and produce "neuropsychiatry."

(b) It makes a difference to the patient whether we take "insanity" as a unit or as a collection of entities: The pragmatic rule decides in favor of a pluralistic view of mental diseases.

(c) The principle of *orderly* exclusion in the diagnosis of complicated cases is of pragmatic value.

(d) Especially is this true of the diagnostic field of neurosyphilis, where it is important to maintain the *non*paretic hypothesis as long as possible in the interest of the patient's therapy.

(e) Opinions might differ as to the advisability of entertaining the hypothesis of focal brain disease before or after the hypothesis of somatic (non-neural) disease in a given case: The pragmatic rule might decide one way for general hospital clinics and the other way for mental clinics.

(f) Schizophrenia should be eliminated before cyclothymia on the pragmatic basis, for a group of schizophrenic symptoms is much more decisive for dementia precox than a group of cyclothymic symptoms is decisive for manic-depressive psychosis.

(g) The pragmatic method decides that in the face of complete ignorance of its true nature, involution-melancholia is better placed in the cyclothymic (manic-depressive) group than in the senile-senescent group, if it is to be placed in either group.

THE RELATION OF GLYCOGEN TO THE PATHOLOGIC CHANGES IN PANCREATIC DIABETES*

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In a previous article evidence was given that the pancreatic diabetic state is a condition in which little or no glycogen is formed from the ingested glucose. In order to make clear the argument following in this article, we will restate our former conclusion—"the pancreatic state of diabetes is a condition where, by failure of the pancreatic internal secretion, glucose is not rapidly enough built into glycogen. By failure to synthesize glucose into glycogen and so remove the glucose from the blood, there results a hyperglycemia and glycosuria." This absence of glycogen in the tissues I shall offer evidences for in this article, accounts for the associated pathologic changes of diabetes such as fatty degeneration and acetonuria.

The importance of glycogen in the prevention of fatty changes of the liver and tissues has been recognized before (Rosenfeld;[1] Graham[2, 3, 4, 5]). In the work of these two observers it was found that the fatty degeneration following such poisonings as mercury, chloroform, was largely prevented by the previously administered diet rich in carbohydrates. Both, in their explanation of the beneficial effect of carbohydrate, came to the conclusion that it was a faulty oxidation of fats when carbohydrates were not being burned. I believe that it is not a question of oxidation directly, but one depending upon the hydrophilic property of glycogen.

Still other observers have called attention to the fatty change when glycogen had disappeared from the cell (Starling,[6] Stolibno). So marked was this fatty degeneration in the absence of glycogen that there was formulated a belief that glycogen and fat existed in a cell only in an *inverse ratio* to each other. Why this was apparently so is easily explained upon the colloidal properties of glycogen and the difficulty in staining fat in a highly dispersed form as it exists in an emulsified state.

GLYCOGEN AND EMULSION

M. H. Fischer[7] has expressed the view that the fat of the tissue is held in an emulsified state by means of proteins; and that the power to emulsify fat is dependent upon the hydrophilic nature of the colloid (protein). We may add that glycogen also is a hydrophilic colloid and as such has a better emulsifying power for the services of the biological kingdom because it is capable of holding more oil or fat than protein, and is more resistant to acids, alkalies and salts. In a system with protein and fat, such as a protein-glycogen-fat emulsion, its stabilizing properties are still noticeable by making the complete system more stable. This is shown by the following experiments with three types of emulsions:

*From the Pathologic Department of the University of Cincinnati.

A.		B.		C.	
Casein	2 gm.	Casein	1 gm.	Glycogen	2 gm.
N/20 — Sodium Carb.	20 c.c.	Glycogen	1 gm.	N/20 — Sodium Carb.	20 c.c.
Oil (cotton seed)	30 c.c.	N/20 — Sodium Carb.	20 c.c.	Oil (cotton seed)	30 c.c.
		Oil (cotton seed)	30 c.c.		

In the proportions given above, the emulsion A (protein fat) is a firm mixture; B (protein-glycogen-fat) rather a liquid; and C (glycogen fat) is a liquid. The pure emulsions, though made with the yellow cotton-seed oil, are pure white in color.

EMULSIFIED FATS AND STAINS

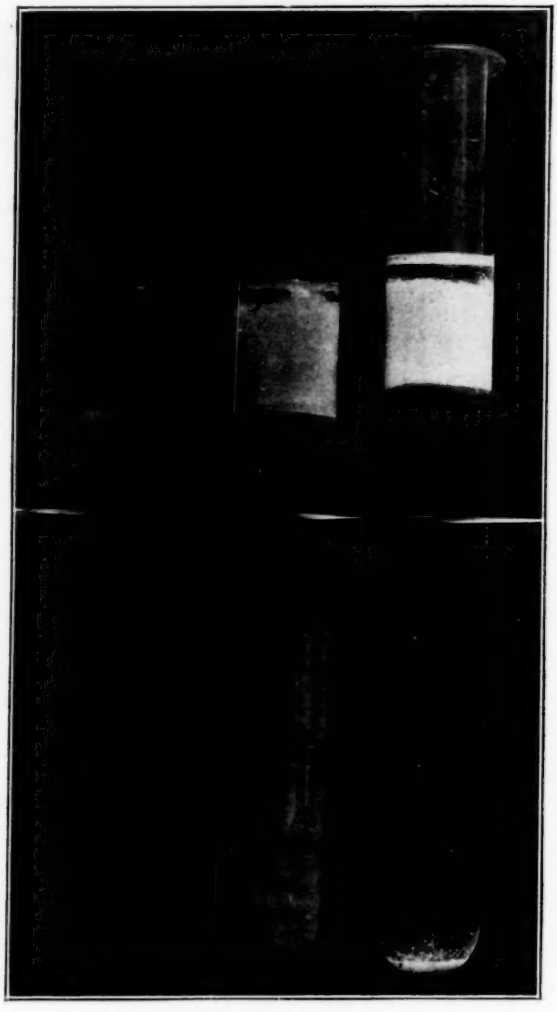
M. H. Fischer[7] has called attention to the fact that when fat is finely dispersed as in the emulsion state it does not show the stains, scarlet red and sudan iii. Not only does the fat not respond to the stains, but glycogen, which stains red with iodine (a method used to indicate the presence of glycogen), does not stain when in the emulsified state. An emulsion similar to C (glycogen-oil) was made, but in place of cotton-seed oil, an oil that stained a deep cherry with iodine was used. This emulsion could not be stained in any manner with iodine; neither the glycogen nor the oil would show the red stain of iodine. Oil was then taken and stained a deep cherry red with iodine and then emulsified by glycogen. The resulting emulsion was as though no iodine had been added, a pure white.

It is this failure of fat to stain in the fine dispersion of an emulsion that has led to the belief of the *inverse ratio* of glycogen and fat in tissues. When glycogen is present the emulsion state is normal and the fat (there in large quantities) does not stain; but as the glycogen disappears from the cells the fat is permitted to coalesce into such sized particles as are capable of showing the stains. The stains do not show an accumulation of fat, as Stolibno, in observing phosphorus poisoning, said, "there is an increase in the fat content of the liver formed at the expense of the carbohydrate constituents of the cell, for with the increase of fat there is a relative decrease in glycogen;" but the stains do show a breaking emulsion with coalescing of the fat particle because the glycogen, a stabilizing agent against acids and salts when there, is being hydrolyzed out. It is this breaking of the emulsion, protein-glycogen-fat, by the hydrolysis of glycogen, that stains and lends an appparent inverse ratio presence of fat and glycogen. Rosenfeld[10] found that the fat chemically estimated in fatty degenerated livers was actually less than normal.

GLYCOGEN AS AN EMULSIFYING AGENT

The amount of oil that an emulsifying agent will hold may be taken at the point where the oil characters begin to appear, such as a greasy feel or a yellowish cast of color to the emulsion. This is at the point that M. H. Fischer[9] calls the change from the protein-oil to the oil-protein emulsion. In the former the protein is considered as the dispersion system, and the oil the dispersed; in the second, the oil has become the dispersion means and the protein the dispersed. A comparison between a protein type and a glycogen type of emulsifying agent shows a marked difference in the oil holding properties of the two.

In the type of an emulsion where protein is used as the dispersing means, less oil is held than in one where glycogen is used. In A, 2 gm. of protein, 20 c.c. of N/20 sodium carbonate, the oil began to appear as the external phase when 50 c.c. of oil were added: but in C, 2 gm. of glycogen, we were able to add before the oil began to appear as the external phase, as much as 90 c.c. of oil.



A. *B.* *C.*

Fig. 1.

The addition of glycogen to a protein oil emulsion raises the quantity of oil that may be emulsified.

GLYCOGEN AND ACIDS

The stability of an emulsion depends upon the relative values of oil, water, and hydrophilic colloid. If the ability of the colloid to hold water be changed, as by dehydration (by acids, alkalies or salts) so that the combined water be-

comes separated, it permits the coalescing of the fat and a breaking of the emulsion.

The breaking of the three types of emulsions by acids depends upon the presence of glycogen in the system. Glycogen as a stabilizing agent in the emulsion adds to the system a strong element of resistance to acids. The protein-fat system is readily broken by the addition of strong acid but the glycogen fat is with great difficulty broken. Fig. 1 shows the behavior of the three types of emulsion (see above, A, B, C). A has had added to it just sufficient hydrochloric acid to cause its breaking. B has had twice the same amount as A, and C has had four times the amount of hydrochloric acid. The emulsion A is completely separated into protein, water and fat. B has been changed very little, while C continues to hold its emulsion form. The addition of glycogen gives to the emulsion a stabilizing power against the breaking by acids.

It is this stabilization by glycogen that in the body serves to prevent fatty degeneration, or dissolution of the cell, as long as glycogen is present, but when the glycogen is hydrolyzed by acids, the protein-fat cell breaks easily into edematous protein and free fat, which we interpret as fatty degeneration.

GLYCOGEN IN DISEASE

Bearing in mind the two important properties, resistance to acids, salts, etc., and emulsifying power, given to an emulsion by glycogen, we find an easy and unstrained explanation of the relation of fat and glycogen in disease.

Rosenfeld[11] observed several points of considerable interest bearing upon such an interpretation as I have given. (1) Various poisons, phosphorus, arsenic, mercury, chloroform, produce always a fatty liver, and in every instance such a liver is glycogen-free. This condition is also true in pancreatic extirpation. (2) Carbohydrates, when fed, prevent a fatty liver. He explained this upon the belief that fats are burned with difficulty without a simultaneous oxidation of carbohydrate, and that in these cases oxidation is seriously lowered. Lusk,[12] however, found the metabolism increased in phosphorus poisoning.

What I believe takes place is that acids formed through the action of the poisoning, hydrolyze the glycogen (as witnessed by hyperglycemia and glycosuria), then causes a separation of the protein-fat emulsion or system that remains. While glycogen is present, the system protein-glycogen-fat is broken by acid only with difficulty, and glycogen is maintained in the system by carbohydrate feeding. I would add here that glycogen is maintained in the system or cell only when the equation glucose $\rightleftharpoons$ glycogen takes place in a medium of right reaction and such a reaction can not be acid. Graham[13, 14, 15] observed the protective value of glycogen against fatty degeneration of the liver.

In the treatment of poisonings such as from mercury, chloroform, etc., the patient should first be alkalinized to make it possible for the reaction to go from glucose to glycogen, then fed carbohydrates in plenty to furnish glucose from which to build a protein-glycogen-fat system that is stable.

FATTY DEGENERATION IN DIABETES

There is little difference between the foregoing fat pathology in the poisonings and in diabetes. In the poisonings the glycogen is hydrolyzed from the pro-

tein-glycogen-fat system, leaving the easily separated protein-fat, while in diabetes there is little glycogen formed, and therefore the emulsion of the diabetes is always a protein-fat emulsion. Consequently feeding alkalies and carbohydrates is of only small value because of the failure to form glycogen from glucose—a reaction which depends upon the internal secretion of the pancreas and is at fault in pancreatic diabetes.

HYPERGLYCEMIA

In all acute fevers, typhoid, pneumonia, etc., Heger[16] found a hyperglycemia. In death after such fever we find the organs have all undergone a fatty degen-

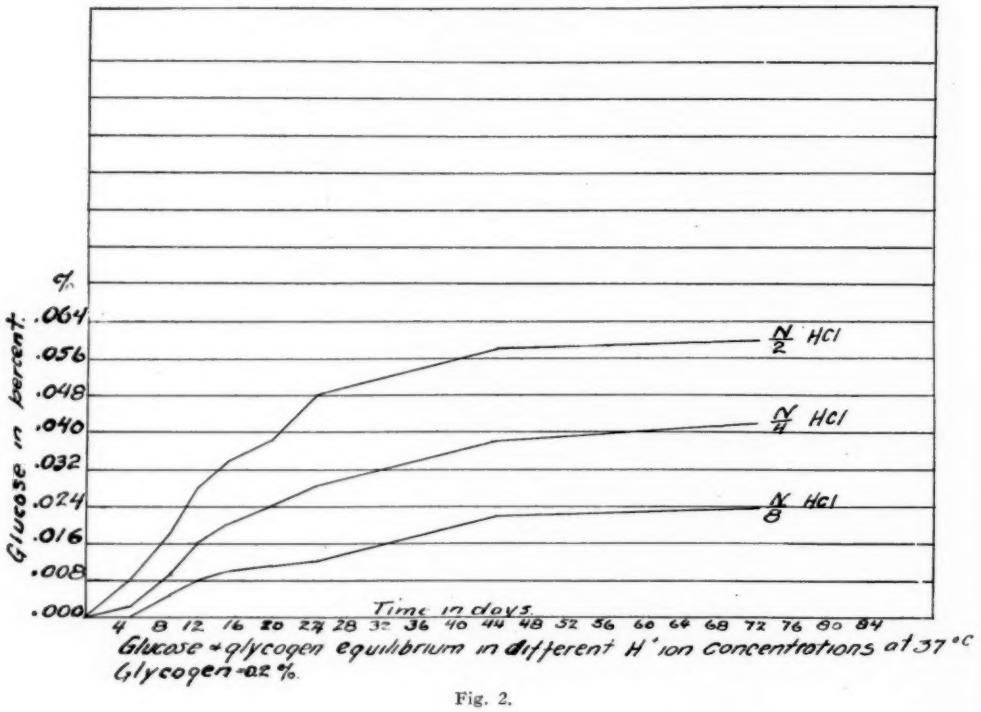


Fig. 2.

eration. In nephritis, Hopkins and Cole[17] found a hyperglycemia. Williams and Humphreys[18] in 80 cases found the blood sugar high in proportion to the gravity of the disease, and in the state of coma the blood sugar rose as high as in diabetes. These conditions, I believe, follow the same law as in mercury and similar poisonings; i.e., it is the result of the catalytic power of the hydrogen ion to shift the equilibrium point between glycogen and glucose.

As the hydrogen ion increases in effective concentration, the reaction shifts towards the glucose side. The shifting may take place to such an extent that the glucose will rise high enough to reach the kidney level. Glycosuria is found in fevers and nephritis. The shifting of the equilibrium of glucose from glycogen by the catalytic power of the hydrogen ion is almost in a direct proportion to the increase of the concentration of the ion.[19] In mercury and chloroform the shifting is only more severe toward glucose, but otherwise the chemical law in

the poisonings and in the fevers is one and the same law. In nephritis and the fevers, fatty degeneration is always present and glycogen is absent. The shifting of the glycogen towards glucose, gives an increase of glucose concentration to the cell, and as the glycogen disappears, the protein-fat system remaining is separated easily by the acids, and gives likewise an increase of fat to the cell. It is the increase of fat and glucose concentration that gives the increase in metabolism. Fig. 2 gives the rate of hydrolysis of glycogen and the different equilibriums of glycogen-glucose in different concentrations of the hydrogen ion.

The pathology associated with diabetes, fatty degeneration and acetonuria has the same underlying cause. Chemical and physicochemical laws govern, as in mercury, phosphorus, chloroform, starvation, nephritis and the fevers. It is the emulsification and stabilizing characteristic of glycogen in the protein-glycogen fat emulsion.

ACETONURIA

An acetonuria is merely the indication of what is taking place in the liver and other tissues. It is the rapid separation of the fat held in the protein-fat emulsion of the body and an overwhelming load of fat delivered to the cell. In mercury, and chloroform, there is a sudden and rapid hydrolysis of the glycogen (a shifting of the glycogen-glucose equilibrium until the glucose concentration in the blood rises high enough to pass through the kidney). This leaves the easily separated protein-fat system which is then broken rapidly by acids with the liberation of a large concentration of fat. It is this increase of glucose and fat upon the cell that gives the increased metabolism found by Lusk. It is another evidence of the law of Guldberg and Wagge that the velocity of a reaction is proportional to their masses. But there is a limit to the oxidizing power of the cell, and the whole of the fat molecule is not burned completely. By this we do not mean that as the molecule of fat reaches the stage of the acetone molecule it is no longer burned, for it is, and a deal is got rid of by the body in that manner; but that in the burning of a large amount of fat, a high concentration of acetone (oxybutyric acid and aceto-acetic acid) is developed and accordingly diffuses through the kidney before it is burned and we detect it. Acetonuria is in reality not a failure in oxidation as we have been accustomed to believe, but an oxidation of too great a load of fat permitting a formation of a high enough concentration of intermediate compound, e.g., acetone, etc., that while a portion is burned completely to CO_2, another portion passes out through the kidney.

Such a condition must manifestly develop where the fat concentration to the cell becomes extremely high. This extreme concentration of fat to the cell may be brought about by either a rapid liberation of the fat already emulsified in the body or by a failure to emulsify the fat of a meal. The first condition is that of starvation, mercury, phosphorus and such poisons, nephritis and fevers; the second is that of diabetes. In this last disease, glycogen is not synthesized and stable emulsions are not formed. When too little glycogen is formed as in carbohydrate starvation with fat feeding, the rate of emulsification is too low and the fat reaches the cell in large quantities. Zeller[20] observed when only 5 per cent of the diet of fat and carbohydrate was carbohydrate, acetone bodies appeared in abundance. Fat is normally regulated in its concentration to the cell by emulsi-

fication in the system protein-glycogen-fat, and by the nicety of the dissolution of this system it reaches the cells in the concentration best suited to their need.

LIPEMIA

The condition of lipemia is another inevitable result from the condition of fat in the system of protein-glycogen-fat. After the taking of a heavy fat meal there will appear in the blood, fat sufficient to produce turbidity.[21] Bloor[22] gives a table of the rise in the blood fat after a fat meal.

24	hrs. after food	0.6 % fat
3¼	hrs, after 100 c.c. olive oil	0.73% fat
6¼	hrs. after 100 c.c. olive oil	1.20% fat
8	hrs. after 100 c.c. olive oil	.87% fat

And Lusk[23] calls attention to the fact that the curve of metabolism after a fat meal runs closely parallel to the rise of fat in the blood as found by Bloor. The temporary lipemia found by Bloor is a result of the slow emulsification of fat, while the lipemia of diabetes is the failure to emulsify the fat even at a slow rate. The lipemia of a diabetic will disappear with the elimination of fat in the diet. This change of concentration of the food stuffs to the cell is likewise the cause of the change in the respiratory quotient.

Lusk,[24] and Joslin and Benedict[25] found in diabetes and in phosphorus poisoning that while metabolism had increased the respiratory quotient had become lower than 1.0. Voit[26] modified the law of Guldberg and Wagge and applied it to biology. The rate of oxidation of the cell is increased by an increase of concentration of food to the cell. In phosphorus poisoning and in diabetes we have an increase of food to the cell—in the former, because in the shifting of the equilibrium of glycogen towards glucose, the concentration of the latter is increased. Likewise with the dissolution of the cell by removal of glycogen, the rate of fat liberation is increased. In diabetes the concentration of glucose is high because it is not emulsified. This increase of concentration of food to the cells gives the increase in metabolism. The change of the respiratory quotient is a change in the respective concentrations of fat and glucose to the cell. In the normal person burning carbohydrates the respiratory quotient is 1.0 because the concentration of fats, soaps, and amino acids in proportion to the glucose is relatively low. But as the concentration of fat rises, the respiratory quotient drops and approaches that of fat alone, 0.72. When a mixture of glucose and fat is burned, the quotient must be somewhere between 1.0 and 0.72. If the glucose is high in relation to the fat, the quotient will be close to 1.0 and if low in relation to fat, the quotient is nearer 0.72. In diabetes the quotient can be raised only slightly by the feeding of carbohydrate because the fat concentration can not be lowered by its storage. In sugar starvation the quotient is low because the fat is increased by the dissolution of the protein-glycogen-fat system. When glucose is fed, the system is rebuilt and the fat concentration lowered. But in diabetes there is no appreciable storage of fat by emulsification, and the feeding of carbohydrates can have but little effect. Similarly whenever the normal concentrations of glucose, soap (fats) or amino acids are altered about or in the cell the relative oxidation is changed and with it the respiratory quotient.

SUMMARY

Glycogen is a stabilizing colloid in the cell and as such prevents the breaking of the emulsion or fatty degeneration by its resistance to acids, salts, etc.

Glycogen is hydrolyzed by acids, and when hydrolyzed, there is left a protein-fat emulsion that is but poorly resistant against acids.

In diabetes no glycogen is formed, the fat is only slightly emulsified, permitting a high concentration of the fats or soaps to reach the cell and a consequent limited oxidation with the production of the acetone bodies.

The equilibrium of glycogen with glucose is shifted towards the glucose side by the presence of the hydrogen ion, which is the explanation of the high blood sugars in fevers, mercury and phosphorus poisoning, and nephritis.

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PATHOLOGY OF INFLUENZA-PNEUMONIA*

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THE pandemic of acute respiratory disease which swept over the world during 1918 has already furnished a voluminous literature in the shape of reports from numerous sections where it occurred. In reviewing this literature one is impressed with the fact that though the various reports differ in certain minor details, they are remarkably similar in essential points. In spite of the enormous amount of work done by numerous observers in widely separated sections of the country, there has curiously enough been little added to our knowledge of these conditions. The specific etiologic agent of influenza has not been determined to the satisfaction of every one. At a recent meeting of the American Public Health Association, after a thorough and searching effort on the part of some of the ablest men of that eminent gathering, the conclusion reached was that "the microorganism or virus primarily responsible for this disease has not yet been identified."[1]

Pneumonia, the most constant complication of influenza and the most prolific cause of the terrible mortality which accompanied it, has been studied by a great many workers and all are agreed that, although lesions resembling both lobar and bronchopneumonia have been met with, these conditions are not absolutely typical of true lobar or bronchopneumonia. Evidently we are concerned with a peculiar type of pulmonary lesion. No one has yet attempted an exact description and classification of influenza-pneumonia as an entity. This paper is therefore written in an effort to add something to the sum total of the records of the pandemic in the form of a report of the pneumonia occurring at Camp Sherman, Ohio; and in the second place to attempt a logical and orderly classification of the conditions met with, together with our ideas of why they assumed the peculiar and particular character which they did. These conclusions have been reached chiefly through a careful study of the first one hundred postmortems held on cases dying at this camp during the epidemic period, from September 16 to November 15. In all more than 150 cases were examined postmortem, but only the first 100 were selected for careful scrutiny and study as a basis for this report. Helpful suggestions were also derived in the elaboration of these views by a careful review of the reports of similar conditions occurring throughout this country.

During the period from September 16 to November 15, 1918,† there occurred 9,380 cases of influenza at Camp Sherman. Of this number, 7,776 were admitted to the Base Hospital. The incidence of pneumonia from influenza in this camp was 2,827, or 30.13 per cent of all influenza cases. Of the total number of pneumonia cases treated in this hospital, 2,181 cases were admitted as such, while only 646, (8.3 per cent) cases developed from the 7,776 cases of influenza treated in the hospital. The number of deaths occurring from influenza and pneumonia during the period mentioned was 1,091, a mortality in our pneu-

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monias of 38.59 per cent; or as a result of all the influenza occurring in the camp, a mortality of 11.63 per cent.

INFLUENZA-PNEUMONIA

It is questionable whether the term "influenza" should be used in connection with our latest pandemic and applied to the pneumonia following it. However, the designation has been so universally applied in this connection that it would hardly avail to substitute another term for it. Obviously, however, if this name be accepted denoting the disease complex occurring during the epidemic, Pfeiffer's organism, also called Bacillus influenzæ, should not retain that name or be associated as the causative agent of the disease until definitely proved as such.

There seems to be a great diversity of opinion among observers in regard to the exact type of pneumonia occurring as a complication of influenza. Some speak of the lesion as a bronchopneumonia which in severe cases developed a conglomerate character simulating lobar pneumonia. McCallum[2] suggests that while these pneumonias are characteristic interstitial broncho in type, the rapid growth of virulent organisms was such that it spread rapidily producing a widespread homogeneous consolidation, owing to the filling of the alveoli with leucocytic exudate loaded with organisms. Nuzum[3] speaks of it as a massive, confluent, pseudolobar pneumonia. Symmers[4] calls attention to the similarity between influenza-pneumonia and Bubonic plague pneumonia. That all are tacitly agreed that we are not dealing with a typical broncho- or a typical lobar pneumonia, is evidenced by the fact that practically every one refers to the pulmonary condition following influenza as either broncho *type* or lobar *type* of pneumonia.

The pulmonary lesion under discussion differs from true lobar pneumonia in that (1) during the stage of red hepatization the cut surface of the involved lung is never dry, but moist and viscid; (2) there is no abrupt transit between the area of consolidation and the surrounding tissue, but rather the whole lobe, and often even the whole of both organs, is involved with a patchy process of smaller or larger areas; (3) the process is not limited as in typical lobar pneumonia to an exudation within the alveoli, but extends itself to the interstitial tissue including blood vessels, lymphatics, and bronchial tubes, resulting in great damage to all these structures, and ending not in resolution but in extensive organization and pulmonary fibrosis; (4) the presence, in many cases, of enormous numbers of large mononuclear wandering cells in the earlier stages of involvement.

It is an interesting fact to note the similarity that exists between influenza and influenza-pneumonia, on the one hand, and such exanthemata as typhoid, measles, purpura hemorrhagica, and certain chemical poisonings, such as benzol, menthol, sulphanol, and so forth, on the other. All show a blood picture varying from a slight reduction in the total leucocyte count, to even a severe leucopenia. McCallum[5] and others have noted the similarity existing between the pneumonias occurring as a complication of measles and of influenza. Typhoid pneumonia and the postinfluenzal pneumonias are similar, in that the large mononuclear wandering cell, or endothelial leucocyte, which is characteristic of typhoid lesions is found conspicuously in the latter condition.

Of the one hundred cases selected for study, necropsies of the first twenty were performed by Wheeler,[6] and the gross findings reported by him. As this

series included some of the earliest cases dying as the result of influenza, they were of peculiar interest for the purposes of this study. Careful microscopic study was made in all these cases by the author.

In the diagnosis of our pneumonias an attempt was made to group them after the fashion generally used in reports coming from other army camps, i.e., 1, acute pulmonary edema; 2 bronchopneumonia, (a), interstitial type, (b), lobular type; 3, lobar pneumonia type. Table I shows the incidence, distribution and stages found.

PULMONARY EDEMA

A number of writers have described this as the very earliest pulmonary lesion causing death in influenza cases. Friedlander, et al.,[6] described such a condition as seen at this camp, and called it "acute inflammatory pulmonary edema."

TABLE I

DISTRIBUTION AND STAGE OF PROCESSES OCCURRING IN ONE HUNDRED AUTOPSIES ON INFLUENZA-PNEUMONIA

TYPE PNEUMONIA / CONDITIONS	BRONCHO-INTERSTITIAL	BRONCHO-LOBULAR	BRONCHO-LOBULAR AND INTERSTITIAL	LOBAR (ALONE)	LOBAR AND BRONCHO-INTERSTITIAL	LOBAR AND BRONCHO-LOBULAR	LOBAR, BRONCHO-INTERSTITIAL AND BRONCHO-LOBULAR
Cases	34	33	12	12	2	5	2
Right side alone	4	5	0	3	0	1	0
Left side alone	2	3	0	2	0	0	0
Bilateral	28	25	12	7	2	4	2
Lower lobes involved	34	25	12	10	2	3	2
Upper lobes involved	31	22	12	9	2	4	2
Middle lobe involved	22	10	8	6	0	4	0
Congestion and edema	7	8	3	5	1	2	0
Red hepatization	20	10	7	5	2	1	1
Gray hepatization	12	9	1	7	2	3	2
Organization	12	6	3	0	0	0	0
Abscess	6	4	0	3	0	1	0
Resolution	0	0	0	0	0	0	1

Lyons[7] described a similar condition under the term, "Hemorrhagic Pneumonitis." Brem, et al.,[8] referred to the condition as "acute hemorrhagic edema."

At the autopsy table one was impressed by the marked cyanosis of the skin, particularly about the face, neck, and fingers. The mouth and nares frequently contained a brownish or reddish, bloody fluid.

The thoracic cavities nearly always contained a definite increase of fluid on the involved sides. This varied considerably in amount from a few c.c. to 1000 c.c. Its color varied from a light brownish-yellow to a dark red, while in character it was serous to serosanguineous.

The visceral pleura generally presented a smooth, glistening appearance, which was, however, rather constantly broken by groups of tiny, petechial, hemorrhagic extravasations beneath the pleura. The spots varied in size from pin-

point to 8 or 10 mm. in diameter, and were in shape generally round, but sometimes irregular. Frequently they conglomerated to form large irregular-shaped areas. They were seen anywhere on the visceral surface, but most frequently on the diaphragmatic and interlobar surfaces, and about the hilus of the lung.

The lungs varied in color, depending upon the degree of involvement, from a deep red through grayish-blue to a light pinkish-gray in the congested areas. The lesions varied depending upon the extent of the process from tiny patchy areas of hemorrhage to large conglomerate areas involving the greater part of a lobe. These areas were increased in consistency, did not crepitate, and pitted on pressure. In no instance was an entire lobe involved by the hemorrhage, air-containing tissue being found in every case on close inspection. These areas were usually found about the periphery of the lobes, or, in cases of interstitial and lobular involvement, between the areas of hemorrhage. Such areas were noted on the surface as nonresilient, emphysematous tissue standing out above the darker, more doughy, hemorrhagic areas. As a result of this air-containing tissue scattered throughout the organ, such a lung when placed in water would float, or at least only partially sink, depending upon the degree of involvement. If, however, a piece of hemorrhagic tissue were cut out from the surrounding organ, it would sink in water. These lungs were large, distended, showing no tendency to collapse, and often showing depression marks of the ribs on their surface. The order of frequency of involvement of the lobes was right lower, left lower, right upper, left upper, and right middle (see Table I). Usually the posterior portion of the lobe was involved, while the anterior portion was frequently free from hemorrhage and congestion, but quite emphysematous. Often, the posterior portions of both upper and lower lobes were involved about equally, while the anterior portions were free. In many instances, the posterior pyramidal portion of the middle lobe was the only part of that lobe involved. Not uncommonly, the posterior portion of both lungs was included in the process.

On section of the lungs, there was an immediate pouring out of dark, bloody, frothy, fluid exudate. The amount of fluid welling from the cut surfaces of the lungs without any undue pressure being exerted on the tissue was often enormous, measuring as much as 200 c.c. in some cases. On scraping away the fluid exudate from the surface, irregular dark-red areas of hemorrhage were seen mottling the whole surface, interspersed with lighter, pinkish-gray areas of the intervening, uninvolved lung tissue. The darker areas were dull, firm, and doughy, with smooth or finely granular surfaces, and varied in size from tiny, scarcely visible specks to large, conglomerate masses occupying the greater part of the lobe. Often, the hemorrhagic areas were limited to a single or a few lobules, and their lobular outline could be distinctly followed. The smaller bronchi stood out above the surrounding surface, their mucous membrane being swollen and edematous. There appeared to be a distinct thickening of their walls, with a consequent narrowing of their lumens. They contained a thin, frothy, blood-tinged fluid, little mucus, and no pus. The trachea and larger bronchi presented much the same appearance as the smaller ones seen on the surface, their mucous membrane being swollen and edematous, and in color, varying from pale pink to a deep, purplish-red.

Microscopically, the lung tissue in the involved areas presented intense congestion and engorgement of the interalveolar capillaries and lymphatics, with extravasation of blood serum and red blood cells into the neighboring alveoli. In fact, the air sacs in these areas were often tensely distended with blood serum and cells. Close to the lining membrane of the alveoli and ducti alveolares a very thin layer of fibrin was seen, in many instances, the only fibrin present. Underneath this, the epithelial lining of the walls was often in a state of necrosis, appearing as a thin, hyaline membrane. Again, air sacs irregularly distributed throughout the hemorrhagic areas were filled with fibrin network, which enmeshed the cellular elements. The walls of the interstitial capillaries and even the larger vessels constantly showed a similar hyaline membrane in which the outline of the individual endothelial cells could no longer be discerned. The hemorrhagic areas were usually sharply delineated from the noninvolved lung tissue. In t he latter areas the air sacs were widely dilated, with thin walls, which, in some instances, were even ruptured. In other areas bordering on the hemorrhagic areas, the lung tissue was in a state of collapse, whole lobules or groups of lobules often being involved. Microorganisms were conspicuous by their absence in these lungs, unless perhaps an occasional organism might be seen in or near the bronchi.

BRONCHOPNEUMONIA TYPE

Both the interstitial and lobular types of bronchopneumonia so ably described by McCallum[9] in cases of pneumonia following measles were met with numerous times. (See Table I.) All stages and degrees of involvement were seen, and did not differ materially from the lesion noted by McCallum. We were, however, very forcibly impressed by the finding of the pneumococcus Types III and IV in culture, and in tissue section from these lungs, as the only organism present, nearly as often as the Streptococcus hemolyticus. (See Table II.) Again, mixed infections of Streptococcus hemolyticus and pneumococcus were found. This is contrary to McCallum's statement that this type of lesion is typical of the hemolytic streptococcus invasion. Thomas[10] mentions finding the pneumococcus Type IV in five such cases at autopsy at Camp Meade. Blanton and Irons,[11] in a report of pneumonias at Camp Custer, state, "Strange as it may seem, there was no difference to be made out in the nature of the process caused by streptococcus, pneumococcus, or influenza bacillus." In a later article, McCallum[5] reports Pfeiffer's organism of influenza as the etiologic agent in the interstitial type of bronchopneumonia. Obviously, we can not therefore accept these types of pneumonia as typical of the invasion of the hemolytic streptococcus. McCallum[2] reports cases of pneumonia resembling closely the lobar pneumonia produced by the pneumococcus occurring in association with typical peribronchial and interstitial changes. From these nothing but the hemolytic streptococcus was isolated. Attention is called to Table II which shows the incidence of the hemolytic streptococcus and pneumococcus in lobar and bronchopneumonia. In fact, it is doubtful whether the type of bacteria isolated from pulmonary tissue in pneumonia is of any value in making a differential diagnosis between broncho- and lobar pneumonia, and it certainly is not between interstitial and lobular types of bronchopneumonia.

INTERSTITIAL BRONCHOPNEUMONIA

Interstitial bronchopneumonia, first described by Kaufman, and first noted in this country by Mathers,[12] was met with in our series thirty-four times as the only type of lesion. The lobular type of bronchopneumonia, referred to by Cole and McCallum[9] in connection with their studies on pneumonia following measles, occurred in our series thirty-three times. These two types occurred together, often in the same lobe, twelve times.

In the earlier cases diagnosed as interstitial bronchopneumonia, the lungs

TABLE II

ORGANISMS AND TYPES OF LESIONS IN ONE HUNDRED CASES OF INFLUENZA-PNEUMONIA

TYPE OF PNEUMONIA / ORGANISMS	HEMOLYTIC STREPTOCOCCUS	PNEUMOCOCCUS TYPE IV	PNEUMOCOCCUS TYPE III	PNEUMOCOCCUS TYPE II	HEMOLYTIC STREPTOCOCCUS AND PNEUMOCOCCUS TYPE IV	HEMOLYTIC STREPTOCOCCUS AND PNEUMOCOCCUS TYPE III	HEMOLYTIC STREPTOCOCCUS AND STAPHYLOCOCCUS	PNEUMOCOCCUS TYPE IV AND PFEIFFER'S BACILLUS	PNEUMOCOCCUS TYPE IV AND STAPHYLOCOCCUS	NON-HEMOLYTIC STREPTOCOCCUS AND PNEUMOCOCCUS TYPE IV	STERILE
Lobar	3	4			2	1					2
Broncho-Interstitial	12	9	2		4	1	2	1	1	1	1
Broncho-Lobular	11	9	2	1	2	1		2	1		4
Broncho-Lobular and Interstitial	3	2		1	2			1			3
Lobar and Broncho-Interstitial	1	1									
Lobar and Broncho-Lobular	2	1			2						
Lobar, Broncho-Lobular and Interstitial		2									

were found to be distended as in the state of full inspiration. Pleural surfaces were frequently smooth and glistening, but usually covered with a thin, finely granular fibrin. On section, the surface of the lung was moist and covered with a yellowish-brown or brownish-red viscid material. Pulmonary tissue was a light grayish-pink color, uniformly dotted with areas two to five millimeters in diameter of yellowish-gray appearance, like disseminated, conglomerate tubercles. These areas were usually surrounded by halos of dark red-colored tissue, and on pressure a tiny drop of pus was expressed from the center of each area. Frequent patchy areas of pulmonary collapse were to be noted. Hyperemia of this lung tissue was very striking.

Microscopically, the bronchioles and infundibuli were filled with polymorphonuclear cells and the invading organisms. These corresponded to the miliary, opaque, yellow spots above noted. Closely hugging the walls of the ducti alveolares and alveoli was a hyaline membrane which was composed of the coagulated necrotic cells of the mucosa. Fibrin in a thin layer frequently covered this process. In these areas, interalveolar tissue was quite swollen, and capillary vessels

thrombosed, their adventitia replaced by a thin, hyaline membrane of necrotic tissue. The lymphatics were plugged with cells. Adjacent alveoli were frequently filled with blood and a few leucocytes. In some places, the process was so limited to the immediate vicinity of the bronchioles that it was designated "acute bronchiolitis."[13]

In somewhat older cases, the cut surface of the lung was dryer and covered with numerous, tiny, firm, projecting nodules, evidently a further process of the one just described. The cross sections of the pus-filled bronchioles gave to the lung surface an appearance not unlike that of miliary tuberculosis. The lung tissue immediately surrounding these miliary foci was consolidated. These areas of consolidation were, if anything, perhaps larger than the areas noted in the previous stage, and, in many instances, had become confluent, forming irregular patchy areas of consolidation through coalescence of the original peribronchial areas. Areas supplied by the involved bronchioles were collapsed and airless. Consolidated areas in the vicinity of the involved bronchi were sometimes surrounded by alveoli in a state of extreme congestion not unlike that seen in the stage of engorgement in lobar pneumonia. The intervening tissue, often collapsed, showed a viscid edema throughout its whole extent.

Microscopically, the bronchioles and infundibuli were seen to be most intensely affected, forming the center of the picture. Their lumen was tightly packed with polymorphonuclear leucocytes, mononuclear wandering cells, and desquamated epithelium. The walls of the bronchi were largely stripped of their lining epithelium. The bronchi together with the tissue immediately surrounding them were intensely swollen, due to infiltration with polymorphonuclear and mononuclear leucocytes, new-formed connective tissue cells, and serum. The infiltration extended to the walls of the adjacent alveoli with consequent thickening of the interalveolar tissue. The alveoli also contained a dense exudate consisting of desquamated flakes from the necrotic mucous lining, polymorphonuclear leucocytes, mononuclear wandering cells, and, in many instances, fibrin plugs. The walls of the sacs were lined with mononuclear cells among which mitotic figures were commonly seen. About the periphery of this process, the exudate was replaced by fluid which was dense and viscid. Organisms were found in the lumen of the bronchi and in the alveolar exudate, but were found most abundantly in the lymphatic channels of this region. The lymphatics were plugged with the infiltrating leucocytes and organisms. Blood vessels were thrombosed, their adventitial tissue being frequently in an advanced state of necrosis, more often infiltrated with leucocytes, lymphoid in nature. In older cases, the exudate in the alveoli and bronchi was found in a process of organization.

LOBULAR BRONCHOPNEUMONIA

In cases diagnosed as lobular bronchopneumonia, the lungs were extremely voluminous and did not collapse when the chest was opened. The pleural surface was frequently mottled with patchy areas of dark bluish-red color, often covered with thin, finely granular fibrin in the very earliest cases. These areas were depressed below the grayish-white colored, intervening surface, or rather the latter were bulging over the consolidated area by reason of the compensatory nonresilient emphysema. On palpation, these areas were felt throughout the entire

organ as nodular masses varying considerably in size. On the cut surface, islands of dark red consolidated lung showed against a paler background of nonelastic, emphysematous pulmonary tissue. These islands appeared as irregular-shaped areas several centimeters in width, sometimes perhaps including only a single lobule, more often a group of several. Their dark red-colored, finely granular, elevated surface was in marked contrast to the intervening grayish-red, crepitating, air-containing, partially collapsed lung tissue. The surface of these lungs was exceedingly moist, the consolidated areas being bathed in large quantities of a viscid, yellowish-red fluid, while the surrounding tissue was covered with a bright-red, frothy fluid. Frequently, these areas were dotted with tiny, yellowish-gray foci not unlike those areas noted in interstitial type. In a somewhat later stage of this type, the process just described, corresponding to the stage of red hepatization in lobar pneumonia, had apparently changed in character to one resembling in many respects the stage of gray hepatization. The cut surface was brownish-gray to grayish-white in color, had lost its finely granular appearance, and was at first dry or nearly so, being covered later with a brownish-red to yellowish-gray sticky, mucopurulent fluid.

Microscopically, the bronchi and bronchioles were found filled with purulent exudate very similar to that seen in interstitial type. The alveoli were tightly packed with leucocytes and fibrin, in some instances, and many organisms. Necrosis of the alveolar walls was constantly seen. The interstitial tissue was swollen and edematous with serum, infiltrating leucocytes, and thrombosed capillaries. The alveolar capillaries were occluded by hyaline, fibrinous thrombi. A little later organization was found to have taken place, the whole area being a mass of granulations. In many cases the granulating tissue was interrupted by areas of coagulated, opaque, yellow, necrotic tissue. These abscesses varied in size from tiny, pinhead areas to abscessed cavities several centimeters in diameter.

LOBAR TYPE OF PNEUMONIA

Twelve cases were met with which were termed lobar *type* of pneumonia. These cases presented larger or smaller areas of distinct consolidation, varying in color depending upon the age of involvement from a dark reddish-brown or brownish-gray to a light gray. In no instance was an entire lobe involved.

Early cases of this pseudolobar process resembled the stage of red hepatization seen in true lobar pneumonia. Pleural surfaces had lost their normal gloss and were covered with a thin, finely granular fibrinous layer, and frequently with subpleural petechia. The involved areas were dense, firm, heavy, airless, and sank in water. These lungs were in size, that of the organ at full inspiration, often with depression marks of the overlying ribs on their surface. On section, the bronchi were reddened with swollen, edematous mucosa, and plugged with a mucosanguineous material. The surface was moist, finely granular, deep red or brownish-red in color. Scraping produced a reddish, sticky fluid. The consolidated area stood out in sharp contrast to the remainder of the lung substance which collapsed, allowing its air content to escape. This latter portion crepitated and oozed a bright red, frothy fluid. Commonly these large areas of deep red consolidation were dotted with numerous miliary, grayish-yellow foci similar to

those noted in the interstitial lobular types. Later cases differed from the earlier in having thicker, fibrinous coats on their surfaces, and a yellowish-gray to purplish-gray color. The cut surface was bathed in a slimy, sticky, mucopurulent fluid.

Microscopically, in the earlier cases, the air sacs were filled with red blood cells, a few white blood cells about the periphery, and, in some cases, considerable fibrin; also many mononuclear wandering cells. Red blood cells often had lost their hemoglobin and were mere shadows. About the walls of the infundibuli and alveoli was constantly found an irregular, hyaline membrane, in which the outline of the individual epithelial cells was lost. Blood vessels and lymphatics were thrombosed and distended with hyaline, coagulated serum, and necrotic cellular debris. Later cases showed the alveoli to be densely packed with polymorphonuclear and endothelial cells, together with partially degenerated red blood cells and coagulated serum. Fibrin was sometimes present and sometimes absent. Many bacteria were found, both in the alveoli and in the interstitial lymphatics. The necrotic epithelium lining of the air sacs and bronchi was largely desquamated and broken up into flaky pieces. The interstitial capillaries and lymphatics were packed with polymorphonuclear and mononuclear wandering cells and bacteria.

ORGANIZATION

Organization has been mentioned by numerous workers as a rather constant feature of influenza-pneumonia, and this has been our experience. Organization in these cases has not differed greatly from that occasionally seen following other types of pneumonia. It has occurred irrespective of the type of pneumonia involved. Resolution occurred only exceptionally in late cases coming to post, and in these it was either incomplete, or entirely lacking. The organized lobe remained more or less completely distended as in the stage of exudation, was heavy, and did not crush easily, being almost as resilient as live rubber. The cut surface was smooth, not granular, and of a moist, glassy appearance. Its color was grayish or reddish-gray, often dotted with yellow, due to alveoli or bronchi still filled with leucocytes; or the young vascular granulations which had replaced the affected bronchi and alveoli immediately adjacent might account in some cases for the small tubercle-like bodies which were seen in gross examination of the lung. The granulating areas varied in size, depending upon the extent of the pneumonic involvement, from areas about the bronchi and vessels, with consequent thickening of the interalveolar tissue, to large areas several centimeters in diameter. The process began with the appearance of the fibroblasts in the interstitial tissue between the air sacs, and in the smaller bronchi and bronchioles. Lymphatic canals were at times found converted into solid vascularized cords of connective tissue. In such areas, the most beautiful, hyaline, fibrous thrombi filled the capillaries of the alveolar walls. From the interstitial areas, fibrosis spread through the alveolar walls into the air sacs, filling these with granulations consisting of embryonic connective tissue and numerous new-formed capillary blood vessels, gradually replacing the fibrin and purulent material in the sacs. During this invasion some of the alveoli still remained filled with purulent material, some often containing large numbers of endothe-

lial cells filled with fat droplets, giving the cut surface the appearance of miliary tuberculosis or tiny miliary abscess formation. In areas of collapsed lung tissue, fibrosis also fused the walls of the collapsed alveoli. In some instances, the combination of atelectasis and organization so completely transformed the lung that one could almost be excused for not recognizing it as pulmonary tissue. As the organized tissue became older, it was found to be infiltrated with numerous plasma cells. There was evidently an attempt at aeration of this healed lung tissue, for, frequently, numerous air spaces, more or less round in shape, were seen lined with epithelial cells and having wide bands of fibrous tissue between them. Still later, such scar tissue evidently contracted, compressing and drawing these new-formed alveoli, as well as the air sacs on the edge of the lesion, into grotesque-shaped, gland-like cavities lined with cubical epithelium. Frequently, the lung tissue was reduced to a dense fibrous mass with few or no epithelial elements left. Again the fibrosis occurred in the form of broad bands, or as isolated islands dotting throughout the entire organ. In some cases it was limited to thickening about the bronchi, together with an overgrowth which accentuated the fibrous trabeculæ. The fibrin deposit on the pleural surfaces was likewise organized, forming a thin or enormously thick, velvety layer of granulations on the pleura. Later, this became organized into a tough, leathery coat which bound the visceral and parietal surfaces together, either over large areas or as fibrous bands. Frequently, such thick, tough, fibrous walls inclosed empyema cavities, preventing inflation of lung tissue, and collapse and healing of the empyema cavity.

All gradations of the above-described pneumonic types and stages were met with. Not infrequently, interstitial, lobular, and lobar types were found in the same case; at times even side by side in the same lobe. Often different parts of a lobe would show different stages of the process, as the acute, hemorrhagic extravasation in one part and pneumonic process in another; or a given part may have progressed to the stage of organization, while another part of a different lobe was still in an earlier stage. Although, in the cases dying within a few hours of acute hemorrhagic edema, this was frequently the predominating lesion, in every instance a careful search demonstrated at least a beginning pneumonic process in some part of the organ.

PLEURAL EFFUSIONS AND EMPYEMA

Pleural effusion occurred in our series in 87 per cent of the cases. Table III shows the character and distribution of these findings. The character of the fluid found in the pleural cavities depended largely upon the age of the pneumonic condition. In the very earliest cases, termed "acute hemorrhagic edema," the pleural surfaces were constantly smooth and glistening, with a greater or less degree of subpleural, hemorrhagic extravasation as described under that condition. In these cases, the fluid was either serous or serosanguineous in character, and varied in amounts from a few c.c. to 1000 c.c. They occurred ten times on the left side, nine times on the right, and six times bilateral. In the earliest pneumonic conditions described as "broncho or lobar type" the pleural surfaces were covered with a fibrinous exudate, sometimes over the

TABLE III

CHARACTER AND DISTRIBUTION OF PLEURAL CONDITIONS OCCURRING IN 87 PER CENT OF NECROPSIES ON INFLUENZA-PNEUMONIA

TYPE	LEFT	RIGHT	BILATERAL	TOTAL
Serous	4	3	4	11
Serosanguineous	6	6	2	14
Serofibrinous	6	4	8	18
Fibrinopurulent	15	11	8	34
Purulent	5	3	0	8
Fibrinous	10	11	14	35
Fibrous Adhesions	11	11	9	31
POCKETS				
Apical	3	0	0	3
Mediastinal	2	2	3	7
Diaphragmatic	1	0	0	1
Interlobar	1	2	0	3

area involved alone, often over considerable of the adjacent pleura. In the very earliest cases, this appeared as a very thin, scarcely discernible clouding of the pleura, or a little later as a thin, finely granular, ground-glass appearing surface; or in the older cases by spongy, light, creamy-yellow fibrinous layer up to three centimeters in thickness. The character of the fluid in these cases varied, depending upon the age from a serofibrinous, fibrinopurulent to a thick purulent material. The fibrin appeared in the serofibrinous fluid as flaky or coarsely granular particles. These fluids occurred most frequently on the left side, and bilateral only sixteen times. Walled off pockets were discovered in a number of instances, occurring most frequently in the following order: mediastinal, seven times; apical, three times; interlobar, three times; and diaphragmatic, once. Thirty-five cases showed a dry, fibrinous involvement of the pleura without any increase in fluid content of the cavity. Thirty-one of the hundred cases presented fibrous adhesions of varying extent, including fibrous bands between visceral and parietal pleura, fibrous obliteration of interlobar fissures to adhesions between parts of or entire surfaces such as the diaphragmatic, mediastinal or pericardial. Thirteen cases showed no discernible pleural change other than a few petechial hemorrhagic areas, on either diaphragmatic, interlobar or mediastinal surfaces. Empyema was not diagnosed unless the fluid was serofibrinous, fibrinopurulent or purulent. Fluids of this character were found sixty times. In cases of excessive fluid, large portions of the lung, frequently an entire lobe, were found collapsed, due probably to the pressure of the fluid. These lungs were dark reddish-black in color, the consistency of live rubber, smooth and velvety on pleural and cut surfaces, in some instances showing pneumonic consolidation, nodular and even conglomerate in type; more often showing no consolidation at all. The cut surface of this tissue was dry, smooth and velvety, with bronchi often standing out above the surrounding surface as thickened tubes filled with thick, brownish or purulent exudate.

CONDITIONS OTHER THAN PNEUMONIA

Following is a list of conditions other than pneumonia found at autopsy:

Respiratory conditions other than Pneumonia

Bronchitis

Acute catarrhal	44
Suppurative	56

Pulmonary tuberculosis	8
Pulmonary collapse	12
Pulmonary infarct	1
Circulatory conditions	
Pericarditis, acute	
Serous	35
Serosanguineous	2
Serofibrinous	18
Fibrinopurulent	10
Myocarditis, acute	48
Myocarditis, chronic fibrous	5
Myocardial congestion	23
Acute cardiac dilatation	84
Endocarditis, acute vegetative	6
Valvular nodules	45
Lymph Gland conditions	
Adenitis, acute, simple	
Peribronchial	69
Mediastinal	61
Axillary	8
Inguinal	1
Mesenteric	5
Calcified peribronchial	8
Tuberculous, peribronchial (caseation)	11
Abdominal conditions	
Peritonitis, acute	
Serous	1
Serofibrinous	4
Fibrinopurulent	1
Liver	
Passive congestion	4
Acute congestion	67
Acute cholecystitis	2
Chronic cholecystitis	14
Hepatic cirrhosis	2
Perihepatitis, chronic fibrous	18
Acute hepatitis (focal necrosis)	28
Hepatic tuberculosis	2
Hepatic infarct	1
Spleen	
Acute splenitis, hemorrhagic	29
Splenitis, subacute	2
Chronic interstitial splenitis	1
Acute congestion	56
Perisplenitis, chronic, fibrous	9
Splenitis, tuberculous	2
Splenic infarction	7
Supernumerary spleen	9
Pancreas	
Acute congestion	47
Stomach and Intestines	
Acute congestion	62
Acute gastritis	1
Intestinal adhesions	1
Intestinal obstruction	1

Appendix	
Appendicitis, acute	1
Appendicitis, chronic	36
Genitourinary conditions	
Kidneys	
Nephritis, acute, glomerulo-tubular	52
Nephritis, chronic diffuse	3
Renal tuberculosis	1
Amyloid degeneration	2
Renal infarct, anemic	3
Acute congestion	74
Acute suppurative pyelitis	9
Cystitis, purulent	1
Skin and Subcutaneous tissue conditions	
Skin	
Vesicular dermatitis	15
Pustular dermatitis	2
Jaundice	25
Emphysema	
Subcutaneous	3
Mediastinal	14
Abscess, subcutaneous	3
Rupture of rectus abdominis muscles	6
Head	
Brain	
Abscess	1
Cerebral congestion	3
Cerebral embolism	3
Ear	
Otitis media purulenta	1
Mastoiditis, purulenta	1
Edema of right orbit	1
Pyorrhea alveolaris	7
Subconjunctival hemorrhage	1

The condition of the trachea and larger bronchi very closely simulated that noted in the smaller bronchi and bronchioles. The mucous membrane was nearly always marked by hyperemia, extremely swollen, and deep purplish-red in color. In earlier cases the hyperemic, swollen condition was usually not so marked, and in some the mucosa had nearly a normal pinkish-gray appearance altered only with hemorrhagic petechia, similar to those on the pleural surfaces of the lungs. The content of these tubes was always large in amount, varying in character from a reddish or pinkish, frothy fluid in the earlier cases to a thick, mucopurulent substance in the later cases. In the later there was a partial or complete necrosis of the mucous membrane, while the contents consisted of a comparatively dry exudate composed of polymorphonuclear leucocytes and mononuclear wandering cells, much mucus and varying amounts of fibrin, all in a more or less complete state of disintegration.

Pericarditis was a very frequent finding, occurring fifty-five times, and usually associated with pleural effusions large in amount. Amounts varied from 30 c.c. to 600 c.c. Fluid up to 25 c.c. was considered normal, unless of a pathologic character. Suppurative pericarditis was seen most frequently in late cases as-

sociated with empyema or general sepsis. In the serous type the fatty tissue underneath the pericardium was usually found to be quite edematous.

The right heart showed evidence of acute dilatation in some degree in 84 per cent of cases. This varied from moderate dilatation in which the right auricle and ventricle were filled with thick, tenacious, black and white clot, to perfectly enormous dilatation of the right heart in which the right auriculoventricular orifice measured 16 cm. from cut edge to edge. In these hearts the myocardium on the right was usually flabby and toneless, while that on the left was firm and contracted with little or no blood clot in the cavities. In the earlier cases the myocardium presented a picture of extreme congestion. Later, there was definite evidence of acute inflammatory change with cloudy swelling and granular degeneration, fragmentation, and even polymorphonuclear infiltration. These hearts varied greatly in size, the average weight being 344.5 grams. The largest heart, 589 grams, was found in a case of interstitital bronchopneumonia involving practically 90 per cent of both lungs. The smallest, weight 200 grams, occurred in a case of broncho-interstitial type pneumonia of nineteen days' duration complicated by pulmonary tuberculosis with abscess formation, and amyloid degeneration of the kidney. The valves of the heart frequently presented a glassy, nodular condition along their free borders about the insertions of the chorda tendinæ. This was attributed to the condition of generalized edema about the heart. Fatty degeneration of the aorta was observed in 35 per cent of cases. This was most marked in the older cases and occurred most frequently at the base of the aorta about the openings to the coronary vessels. It occurred here in the form of irregular-shaped plaques raised slightly above the surrounding surface. These plaques measured from 3 mm. to 8 mm. in diameter. Occasionally, similar plaques were found on the arch of the aorta about the openings to the neck vessels. Along the descending aorta the degenerative process assumed the form of fatty streaks lying parallel to the longitudinal axis of the vessel, and most marked about the openings of the intercostal arteries. In only two cases was the aorta involved below the diaphragm. In two cases the fatty degeneration had progressed to an atheromatous state.

Lymph nodes about the hilus and in the mediastinum were usually in an acute inflammatory state, except in the very earlier cases of hemorrhagic edema. In these cases, the picture under the microscope was that of intense engorgement of the lymphatics. In the older cases, however, nodes were enlarged, soft and gelatinous, with glassy edematous appearance on their cut surfaces.

The average weight of the liver was 1805 grams. The largest weighed 2772 grams, and occurred in a case showing an intense congestion of the organ, with widely dilated central and intralobular veins. The liver cells about the central veins showed extreme fatty degeneration and vacuolization. The smallest weighed 906 grams and occurred in a case of interstitial bronchopneumonia and pulmonary tuberculosis. The liver was very generally involved with miliary type of tuberculosis, showing typical tubercle formation with caseation necrosis. The liver cells were extensively involved with fatty degeneration and infiltration, and there was a marked lymphocytic infiltration throughout the entire organ, more particularly noticeable about the vessels. Two rather distinct types of liver involvement were noted in connection with influenza-pneumonia. The one was

termed an acute congestion, and was noted 67 times in our series. This was manifested by enlargement of the entire organ, with a tense capsule, and a purplish-blue surface. The cut surface bulged over the edge of the capsule and was usually a light to dark reddish-brown color. Considerable blood dripped from the cut surface. Microscopically, all blood vessels, afferent and efferent, but more particularly the central veins and intralobular capillaries, were found to be widely dilated.

The second type of liver was usually not so markedly enlarged, and was of a light bluish-gray color, frequently mottled on the surface by pale yellow, irregular-shaped areas. The cut surface of these livers was less bloody, did not bulge over capsule, and was of a light yellowish-brown color, sometimes uniformly so, sometimes distributed in the form of irregular sized and shaped areas throughout the organ. Microscopically, there was found to be quite a marked fatty degeneration of the liver cells, frequently including only a narrow zone about the central vein, often however, involving the entire, or greater portion of the lobule. These yellowish livers were frequently associated with jaundice, but not constantly so. These cases were termed "acute hepatitis," twenty-eight in all being found. Four cases of typical nutmeg liver, or passive congestion, were seen.

Conditions most frequently seen in the spleen coincidently with influenza-pneumonia were acute congestion and acute hemorrhagic splenitis. The cases termed "acute congestion" occurred 56 times, and were manifested by an increase in size, at times enormously so, tense consistency, dark red color, eversion of cut edge, and soft friable pulp substance. The prominent Malpighian bodies and trabeculations were noteworthy. Microscopically, sinuses were seen to be intensely engorged with blood, and the Malpighian bodies swollen and edematous.

In acute hemorrhagic splenitis, the organ was comparatively pale, only slightly or moderately increased in size, and frequently marked on the surface with light grayish-pink, soft areas. On section, the cut surface was either uniformly a light grayish-pink color, soft, and friable, or else presented numerous areas of this appearance several centimeters in diameter and irregular in outline. The Malpighian corpuscles and trabeculations were indistinctly seen or entirely obliterated. Microscopically, this splenic tissue was seen to consist of an extravasation of blood elements into the splenic substance, sometimes involving and destroying even the Malpighian bodies. These areas sometimes were minute in size; again, including a large part of splenic tissue. In some instances the red cells were in remarkably fresh state; again, they were decidedly degenerated and the area infiltrated with polymorphonuclear and large mononuclear wandering cells. Definite splenic infarcts were noted in 7 per cent of the cases. The average weight of these spleens was 170 grams. The largest was 673 grams, occurring in a case of interstitial bronchopneumonia, and was a combination of the congestion and acute splenitis types. The smallest weighed 30 grams, and occurred in a case of combined broncho- and lobar types of pneumonia. This was noted as an acute hemorrhagic splenitis.

Acute congestive condition of the kidneys was noted 74 times. Acute nephritis of a glomerulo-tubular type was diagnosed 52 times. These kidneys were swollen, showing eversion of their cut edge, the color of the latter being

either an intense purplish-red, or grayish-white. Hemorrhagic extravasations were not infrequent. Cloudy swelling and granular degeneration of glomerular and tubular epithelium was marked, and, in many instances, desquamation of tubular epithelium was quite extensive. Right kidneys in these cases averaged 169 grams in weight, the largest weighing 315 grams, and occurring in a case of bronchopneumonia, the kidney condition being diagnosed acute glomerulotubular nephritis. The smallest right kidney weighed 84 grams, and was found in a case of broncho-interstitial pneumonia. The kidney was an infantile lobulated type. The left kidneys averaged 161.1 grams in weight. The largest, weighing 348 grams, was seen in a case of interstitial bronchopneumonia with intense renal congestion. The smallest left kidney weighed 60 grams, and occurred in a case of interstitial bronchopneumonia. No lesion could be determined in this kidney other than slight amount of congestion.

Emphysema was noted with striking regularity in cases denoted hemorrhagic edema, and the various types of pneumonia. Quite constantly this was present as a compensatory condition in those parts of the lung tissue not involved by the hemorrhage. In fourteen instances, it was found in the loose aureolar tissue of the mediastinum, and, in three instances, had extravasated to the subcutaneous tissue over the front of the chest and neck. In one case this had become so extensive as to extend over the entire face and neck, down the arms to the hands, over the thorax and abdomen, into the scrotum and over the upper half of both thighs. Clark and Synnott[14] reported twenty such cases occurring in influenza-pneumonia. Brenn, et al.,[8] reported two cases of subcutaneous emphysema found in thirty necropsies done on influenza cases.

A peculiar condition was noted on the skin surface of a number of these cases which was termed a "vesicular dermatitis." It was characterized by tiny, pinhead, water-clear blisters of the epidermis. So thin were these vesicles that they could be rubbed off in passing the hand over the skin surface. They gave one the impression of tiny drops of water resting on the body. They occurred most commonly over the chest and abdomen, but, in some instances, were found over the shoulders and upper arms, neck, and upper thighs. Application of irritant substances to the skin surface was ruled out as a causative factor. Consultation with dermatologists resulted in the conclusion that this was a form of toxic dermatitis. In two instances, the vesicular condition had become pustular. Jaundice was noticed twenty-five times and varied anywhere from a slight icteric condition of the conjunctivæ to a generalized deep saffron yellow. In some instances, this could be accounted for by a condition of acute toxic hepatitis, but, in other cases, no liver disturbance could be found.

Rupture of the rectus muscle occurred so frequently as to attract attention. The separation usually occurred midway between the symphysis pubis and umbilicus, but one case was found where it occurred between the ensiform and umbilicus. In one case it was complete, but usually only involved a few fibers. In four cases the rupture was bilateral. It was usually accompanied by large hematoma underneath the sheath of the rectus. The hemorrhage frequently had dissected downward in front of the bladder. Microscopically, the muscle fibers showed granular degeneration, cloudy swelling, and fragmentation. In later cases, the hematoma and muscle fibers were profusely infiltrated with poly-

morphonuclear leucocytes and mononuclear wandering cells. Frequently, they were localized into definite abscesses.

BACTERIOLOGY

Table IV shows the incidence of the various organisms occurring in our pneumonias. The table is the result of the autopsy examination of the lung, spleen, kidney, pleural and pericardial fluids, and heart's blood. Blocks of tissue were taken from the lung, spleen and kidney after searing the surface

TABLE IV
POSTMORTEM CULTURES FROM ONE HUNDRED CASES OF INFLUENZA-PNEUMONIA

ORGANISM	LUNG	SPLEEN	KIDNEY	PLEURAL FLUID	PERICARDIAL FLUID	HEART'S BLOOD
Pneumococcus Type II	1	0	2	1	1	2
Pneumococcus Type III	7	1	1	2	2	2
Pneumococcus Type IV	50	19	8	26	40	42
Streptococcus Hemolyticus	45	35	0	23	35	36
Pfeiffer's Bacillus	4	0	0	5	0	0
Staphylococcus	2	0	0	0	0	0
Nonhemolytic Streptococcus	1	0	0	0	0	0

with a red-hot spatula. These tissue blocks were macerated in sterile salt solution and planted on blood agar plates and plain broth. Smears also were made from this macerated tissue and stained by Giemsa's and Gram's method. Sections from these various tissues were also stained by Goodpasture's modification of the Gram-Weigert method, which we have found a most excellent stain for demonstrating bacteria in tissue. Pfeiffer's organism is stained very readily by this method. Pleural and pericardial fluids and heart's blood were cultured in plain broth.

Table II is a summary of the organisms occurring in the various types of pneumonia. It is to be noted that hemolytic streptococcus was found alone three times, and hemolytic streptococcus and staphylococcus twice, and pneumococcus Type IV occurring four times. A mixed infection of hemolytic streptococcus and pneumococcus Type IV occurred two times, while the combination of hemolytic streptococcus and pneumococcus Type III occurred once. In interstitial bronchopneumonia type, hemolytic streptococcus was found as the only organism in twelve cases, pneumococcus Type IV in nine cases, and pneumococcus Type III in two cases. Combinations of hemolytic streptococcus and pneumococcus occurred five times, and hemolytic streptococcus and staphylococcus twice, and pneumococcus and Pfeiffer's bacillus once, and pneumococcus and staphylococcus once. In the lobular type of bronchopneumonia, hemolytic streptococcus was the predominating organism eleven times, pneumococcus Type IV nine times, pneumococcus Type III two times, pneumococcus Type II once, hemolytic streptococcus and pneumococcus three times, pneumococcus and Pfeiffer's bacillus two times, and pneumococcus and staphylococcus once.

INFLUENZA-PNEUMONIA AS AN ENTITY

As a result of our studies in influenza-pneumonia, I wish to present the following conception and classification of the condition. Influenza-pneumonia may be defined as a primary, acute, hemorrhagic lesion, interstitial, nodular, or massive in extent, arising from a pulmonary capillary phlebitis with disseminated capillary necrosis due to some toxic agent and resulting in a secondary purulent pneumonia with healing by organization. Primarily and essentially, the pulmonary injury in influenza is an acute hemorrhagic and serous condition, evidently the result of some toxic agent,[13] chemical in nature, whether organic or inorganic it is impossible to say. It is not inconceivable that such toxic agent should emanate from a part remote from the lungs themselves. For example, Pfeiffer's bacillus or some other as yet unidentified organism, localized in the nose or throat, might eliminate a toxin so virulent as to account for the condition under discussion. It is a known fact that toxins eliminated by such organisms as the diphtheria or tetanus bacillus cause disastrous injury in parts of the body remote from the point of localization of the organism. In influenza, the acute hyperemia of the conjunctiva and the intense lividity of the pharynx described as a red fringe, or crescent bordering the hard palate, with minute hemorrhages and a papulovesicular rash in the livid mucosa has been referred to by many observers.[15] One who has seen many of these cases is struck by the fact that there is a decided and severe disturbance in the character of the blood and the circulatory system in general. That such a toxic agent has not only altered the character of the blood, but has affected all tissues that it bathes is reflected in the finding of generalized conditions throughout the whole body. A definite hemoglobinemia has been noted. Hemorrhagic extravasations are found in practically every organ throughout the body, including the musculature. The condition might be compared to that seen in purpura hemorrhagica of a severe type. That the lungs were so severely affected is not surprising when we think of the vulnerability of their anatomic structure to any toxic agent carried in the blood stream. The lung with its delicate network of capillary vessels surrounding the alveoli forms the most susceptible organ of the body for attack. The thrombosis and adventitial necrosis of the pulmonary vessels has been noted above in the descriptions of the lung conditions. Lyons[7] has suggested that the location of the hemorrhage largely in the posterior parts of the lungs—all lobes—is connected with posture as in hypostatic congestion. When we remember the extreme early prostration of these cases and the fact that they are most frequently found "flat on their backs," this suggestion becomes most plausible. On the other hand, it is conceivable that the toxic agent should have reached the lung parenchyma by way of the respiratory tract either in a liquid or gaseous state. The constant finding of necrosis of the lining epithelium of the infundibular and alveolar walls in all types of pneumonia has been noted in our descriptions of these conditions. Goodpasture[13] succinctly states this viewpoint as follows: "The pulmonary injury and reaction being so acute and often widespread, and the fact that in certain very early cases, bacteria of any kind are so scarce or not found at all, make us feel, notwithstanding the demonstration of influenza bacilli in pure culture in the lungs in all but one instance, that at this stage organisms are as yet comparatively few within the alveoli, and

their primary injury is due to a very potent toxic substance elaborated in and disseminated through the larger air passages."*

We consider this primary lesion a serous and hemorrhagic pneumonitis, of toxic origin, starting as a phlebitis of the pulmonary capillaries. The pneumonitis results in the production of multiple infarcts of various sizes throughout the lung. Beginning with the circulatory system, we note an intense engorgement of all the vessels, large and small, but particularly the interalveolar capillaries, arterioles and venules. Vessel walls are intensely swollen and edematous, the adventitia being frequently in a state of necrosis as noted before. In places these have ruptured, filling the neighboring air sacs with erythrocytes and serum. In some instances, this hemorrhagic extravasation is confined largely to the interstitial tissue and to small areas two or three millimeters in diameter about the bronchioles and infundibuli. In other cases, sometimes in other parts of the same organ, even sometimes within the same lobe, are seen areas of hemorrhagic extravasation larger in extent involving an entire, or several lobules. In still other cases, the involvement has become massive, either through conglomeration of the previously described lesions, or because of the severity of the process, and generalized lack of resistance on the part of the lung. In other words, this primary influenzal lesion may be interstitial, nodular, or massive in distribution. Presumably these types of lesions are determined by the amount and virulence of the toxic agent on the one hand, and the resistance of the tissue on the other hand. Possibly the only reason why the entire five lobes do not become uniformly involved in some cases is that death necessarily occurs from lack of air before so complete an involvement can take place. At any rate, it is surprising how extensive the process became in some instances before death intervened. Curiously enough, a careful study of these very earliest lesions fails to discover the presence of any organism in the hemorrhagic areas, either by culture or by tissue sections. The rather sharp differentiation between the areas of hemorrhagic extravasation and the uninvolved tissue is also notably in favor of this conception. Obviously, the interstitial and nodular types have not been seen in this stage except in connection with the conglomerate types, as they alone would hardly be extensive enough to cause death. In any event, these types of hemorrhagic lesion form an excellent foundation for the secondary pneumonic lesion.

Thus the condition of multiple pulmonary infarction, interstitial, nodular, or conglomerate in type forms the starting point, out of which grows the secondary stage of influenza-pneumonia. The injured pulmonary vessels accompanying the bronchi and bronchioles down to their final ramifications and surrounding the alveoli with a delicate network of capillaries make the whole bronchial tree a point of markedly lowered resistance to any pathogenic organism which might gain access to the respiratory tract, or to those bacteria normally present there. The areas consisting of clotted blood and serum form a most excellent medium for the rapid growth of any organism that should gain access to it. Very likely these organisms are planted through the respiratory tract. That this is probable is evidenced also by the fact that the more common organisms found normally in

*While this paper was in the course of preparation LeCount (Jour. Am. Med. Assn., lxxii, No. 21, p. 1519) called attention to the "disseminated necrosis" of the pulmonary capillaries of the lung in influenza-pneumonia noted above, and concluded from his studies that the evidence was in favor of this condition being prodromal to the hemorrhage rather than secondary to the pneumonia. This is in keeping with the above conception of the pneumonia lesion.

the nose and throats of individuals have been the ones most frequently concerned in the so-called secondary influenza-pneumonias. The diversity of the organisms found in the pneumonias occurring in various sections of this country is an additional argument in favor of this conception. Seemingly, the organism, or organisms, predominantly present in the nose and throat of individuals in any particular section of the country is the organism predominantly found in cultures and tissue sections from the lungs of pneumonias in that section. Thus from one community Pfeiffer's bacillus[16] has been found in the majority of instances (as high as 82.6 per cent of lung cultures), while in others, pneumococcus type III or IV, hemolytic streptococcus,[7] Streptococcus viridans, staphylococcus, micrococcus catarrhalis, or Friedländer's bacillus[16] have been found predominating. That this is so, and that recognized reliable workers have made such reports from different sections of the country increases the strength of the foregoing statement.

It is also conceivable that some at least of these pneumonias derived their secondary invaders by way of the blood stream. Positive blood cultures have been frequently obtained from these cases. Ritchie and Goehrings[17] found that in cases of marked prostration, septicemia was very common, and that the more common bacterial inhabitants of the body, such as staphylococcus, streptococcus, etc., were the most common invaders. Oberndorfer[18] has defined influenza as a bacteremia.

Obviously, the type of the secondary pneumonia would largely be determined in the beginning, at least, by the type of the primary condition, i.e., interstitial, nodular, or conglomerate. In the very earliest cases of invasion the areas of infarction are seen to be in a process of invasion by the polymorphonuclear leucocyte, and the large mononuclear wandering cell on the one hand, and the secondary invading organism on the other hand. Red blood cells are in a process of disintegration, in many instances, having lost their hemoglobin, and appearing as mere shadows. Still later they have lost even their shadowy outline. This corresponds roughly to the stage of red hepatization mentioned in the lobular and lobar types previously described. Somewhat later, the lesions are characterized by a mass of polymorphonuclear and endothelial cells, together with a yellowish-gray, sometimes mucoid, fluid. This corresponds to the stage of gray hepatization, and is simply a purulent stage of this secondary pneumonia. All types, interstitial, nodular, and massive, pass through these stages, differing only one from the other in extent of the lesion. True, there is an extension in many instances of this secondary pneumonia beyond the limits of the primary infarction, due to the activity of the secondary process. In these cases, the former uninvolved area becomes intensely congested about the periphery of the hemorrhagic area, and gradually passes through the stages of engorgement, red and gray hepatization.

Mention already has been made of the extensive damage done to the lung tissue and the resulting organization. Coincidently with the beginning of organization, there is a walling off of the various purulent areas by the more resistant tissue with the formation of abscesses varying in size from the miliary foci seen in the interstitial type to areas several centimeters in diameter seen in the nodular and conglomerate types. As organization proceeds, these abscess areas are replaced by granulations rarely persisting as pulmonary abscess cavities. The areas

not primarily involved in the hemorrhagic process, but secondarily invaded as extension from the primary foci, are more prone to undergo typical resolution, the damage to the lung tissue seemingly having not been as destructive here.

Following is a schematic outline of the classification and conception of influenza-pneumonia as just discussed:

	Division as to causative agent	Types with respect to extent	Stages in point of time
INFLUENZA-PNEUMONIA	I. Primary (some unknown toxic agent)	a. Interstitial and peribronchial b. Nodular or lobular c. Massive or conglomerate	1. Serous 2. Hemorrhagic
	II. Secondary (the predominating organism occurring in the nose and throat of the individuals of a given section)	a. Interstitial b. Nodular c. Massive	1. Purulent infiltration (hemorrhagic) 2. Abscess formation 3. Organization

CONCLUSIONS

The pneumococcus and hemolytic streptococcus were the most frequent secondary invaders found in the lungs at autopsy in the pneumonias at Camp Sherman. Pfeiffer's bacillus was found in only 4 per cent of the cases.

Interstitial and lobular bronchopneumonia can not be regarded as typical lesions resulting from the invasion by the hemolytic streptococcus. The pneumococcus was found to be the only invader just as frequently as the hemolytic streptococcus in these types of pneumonias. In fact, it is doubtful whether the type of organism isolated from pulmonary tissue in pneumonia is of any great value in determining the type of pneumonia present, for the type of organism concerned and the type of lesion in the lung are decidedly variable at different times even at the same station.

Influenza-pneumonia is primarly an acute, hemorrhagic lesion, interstitial, nodular, or massive in extent, rising from a pulmonary capillary phlebitis with disseminated capillary necrosis due to some toxic agent and resulting in a secondary purulent pneumonia with healing by organization.

That organism or organisms predominately present in nose or throat in the individuals in any particular section of the country is the organism most commonly found in cultures and tissue sections from the lungs of secondary pneumonias in that region.

Empyema and pericarditis are frequent complications.

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THE CHOICE OF SERA IN THE TREATMENT OF MENINGOCOCCUS SEPSIS*

By M. B. Cohen, M.D., Ashland, Ohio

THE epidemics of meningococcus sepsis which have occurred in army cantonments have necessitated an intensive study of meningitis therapy.

Following the success obtained in the treatment of this disease by Flexner and Jobling by the intraspinal injection of immune serum, a number of observers have noticed variations in the therapeutic result following the use of different sera. These differences were explained on the basis of the existence of various serologically different strains of the meningococcus.

Studies by the Royal Army Medical Corps in England, the Pasteur Institute in France, and the Rockefeller Institute in the United States have shown that the group of meningococcus bacteria is a heterogeneous one, and that there are at least four strains or varieties that can be separated by serologic methods. Though each group of workers claims to include in its classification the serologic types of the others, it is, at the present time, impossible to state the exact relationship between these various classifications.

The various commercial polyvalent antimeningococcic sera are made from a number of strains of meningococcus isolated from the spinal fluids of cases of meningitis, and are supposed to contain immune bodies for the four main groups. In spite of the polyvalency of the sera, however, many cases have not responded properly to serum treatment. Clinicians have been in the habit of changing sera when proper results were not obtained, as their experience had shown that the change was frequently associated with clinical improvement. This experience has led them to condemn the sera of some manufacturers as unreliable.

Some clinicians have suggested that the agglutination titer of the various commercial sera in stock be determined for the organism isolated from the patient. Until the present, however, such tests have been impractical, because of the difficulties in isolating and cultivating the meningococcus in sufficient amount with such rapidity that a report could be sent to the clinician within forty-eight hours after the patient's admission to the hospital.

That such growth can be obtained in less than twenty-four hours, by smearing the spinal fluid on any suitably enriched medium, such as blood agar or sheep serum agar, has been recently demonstrated by the author and Fleming.†

As most sera are at present tested for potency by agglutination reactions against known strains, and as this method is reasonably rapid and is less subject to error than the other available serologic procedures, the agglutination reaction was selected as an index of potency of a serum against the organism isolated from the spinal fluid of the patient.

Each available commercial serum was tested in dilutions of 1-50; 1-100; 1-200; 1-400; 1-800; and 1-1600 with a suspension of meningococcus isolated

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†Jour. Infect. Dis., 1918, xxiii, 337.

from each patient as described above. Controls of saline suspension and horse serum were included in each series. The following protocol serves to illustrate the method and result.

AGGLUTINATION OF MENINGOCOCCUS STRAIN NO. 101 ISOLATED AT PARTIAL TENSION ON BLOOD AGAR. SUSPENSION MADE FROM 18 HOUR CULTURE AT 37° C. AGGLUTINATION CARRIED OUT AT 55° C. FOR 18 HOURS

COMMERCIAL SERUM	1-50	1-100	1-200	1-400	1-800	1-1600	1-50 HORSE	SALINE
A	** **	** **	**	*	–	–	–	–
B	** **	** *	*	–	–	–	–	–
C	**	*	–	–	–	–	–	–
D	** **	** **	** **	** *	*	–	–	–
E	** *	**	*	–	–	–	–	–

*Positive. –Negative.

From the foregoing protocol it is evident that Serum D would be the best to employ for the case in question, whereas Serum C would be considered the least reliable.

When a new patient was admitted to the meningitis ward, the laboratory was notified. While waiting for the arrival of the bacteriologist, the clinician made a lumbar puncture and collected a specimen of spinal fluid. The bacteriologist, upon his arrival, removed 10 to 20 c.c. of blood from the median basilic vein for a blood culture, and immediately returned to the laboratory with both specimens. The clinician used his own judgment as to treatment based on a preliminary bacteriologic report, using any available serum, until he received a report from the laboratory on the agglutination titer of the various sera available against the strain isolated from the case in question. He would then choose the serum which had the highest titer for further treatment of the patient.

The procedure described above has been found by actual test to be practical and very satisfactory. It requires for its success the full cooperation between the clinical and laboratory services.

LABORATORY METHODS

ABOUT A NEW STOMACH EXAMINER, BASED ON THE HYDRAULIC PRINCIPLE

By Dr. Komanosuke Togami, Igakuhakushi, Fukuoka, Japan

TO OBTAIN the stomach fluid, the expression method is considerably employed. This method is successful in cases in which the stomach secretion is abundant, but is often a failure in those with diminished secretion or pronounced atony. Apart from this, it requires a long time to take the stomach contents, and sometimes it causes a damage of the mucus of the stomach. Therefore it is necessary to apply the negative pressure to obtain the contents of the stomach, in every case of the stomach examination. For this purpose we have Boas' bulb and the Potain's apparatus. The former shows sometimes insufficiency of the negative pressure, while the latter is very circumstantial and may cause at times serious damage of the mucus of the stomach, by producing heedlessly unnecessary negative pressure.

I have lately designed a new aspirating apparatus, by which the negative pressure produced at once automatically by water pressure, and the variation of the pressure can be measured by a manometer at every moment. The procedure is very simple and one can aspirate the stomach contents safely and quickly. Moreover the apparatus can be applied for several important examinations of the stomach, as shown in the following.

In the first place it will be necessary to give a description of the construction of this apparatus and make some remarks upon the hydraulic principle employed.

A closed vessel *A* and an open vessel *B* are placed in a row, and the closed vessel *A*, having a capacity of about 3000 c.c., provided at the lower part with a discharge pipe *K* and a cock *K'*, and fitted at the upper part with a bent pipe (*a*), which is divided in three branches *R*, *U* and *V* (Fig. 1). The upper branch *R* is connected with the air gauge *E*, and the other two with the closed vessels *C* and *D*, arranged on the lower stage. The closed vessel *C* is fitted at the lower part with a discharge pipe *F* and a cock *F'* and provided at the upper part with a connecting pipe *M* which connects the closed vessels *C* and *D*. The closed vessel *D* is fitted at the lower part with a discharge pipe *H* and a cock *H'* and provided at the upper part with a joint pipe *P*. The open vessel *B*, having a capacity of about 4000 c.c., is provided at the lower part with a discharge pipe *G* and a cock *G'* this being connected in a T-shape with a connecting pipe *Q* of an elevating vessel *J*, and the communicating pipe *Q* is fitted with a cock *Q'*, and its further end is connected with a cock *N'* of a communicating pipe *N*.

By opening *K'*, after closing *K'*, *F'*, *H'* and the upper cocks of *A*, *C*, *D* and the pipe *P*, the water in the closed vessel *A* will run down through the discharge pipe *K*. With the lowering of the water level in the vessel *A*, the air in the vessel *C* and *D* will increase its volume. According to Mariotte's law the pressure is reciprocal to the volume and with an increase of the volume of the air the pressure of the air will be gradually reduced. When the sum of the pressure of the air in the vessel *A* and of the water in the vessel *A* and the pipe *K* is equal to atmospheric pressure, the water will no longer run out through the discharge pipe *K*, and the water level will remain constant. On the other hand, the diminution of the air pressure in the vessel *C* and *D* can be read by the difference of the levels of the mercury of the air gauge, and to produce a greater negative pressure, it will be necessary either to raise the closed vessel *A* to a higher position or to lengthen the discharge pipe *K*, in order to increase the height of the water column.

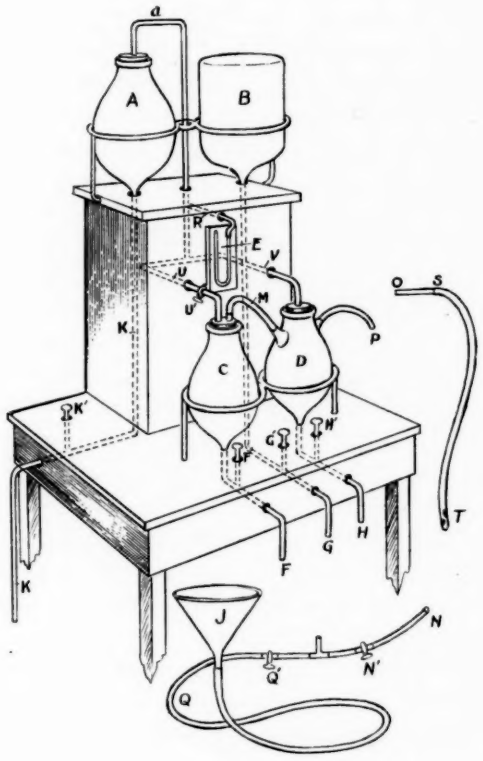

Fig. 1.

PREPARATIONS FOR OPERATIONS

Before performing operations the following points should be noted.

1. The closed vessel *A* and the open vessel *B* should be filled with water.

2. The upper parts of all closed vessels *A*, *C*, *D* and the cocks *K'*, *F'*, *G'* and *H'* should be closed air-tight.

3. In case of lavage, the lotion should be poured into the open vessel *B* in place of water. If one operates only for the aspiration of the gastric fluid, it is not necessary to fill the vessel *B* with water.

OPERATIONS

1. The aspiration of the gastric contents.

After connecting *P* and *S*, the tube *T* should be introduced into the stomach, and the cock *K'* opened. The water in the vessel *A* will run down through the discharge pipe *K* and there arise a negative pressure in the closed vessels *C* and *D*, which is read by the manometer. When there is fluid in the stomach, it will be at once drawn up into the closed vessel *D*, going further into the closed vessel *C*, in case the vessel is full of liquid through the pipe *M*. After taking the stomach contents, *P* and *O* should be separated and the tube drawn out from the stomach. When we open the cocks *H'* and *F'*, the stomach contents in the vessels *C* and *D* can be taken in a receptacle for the examination.

To take the fluid out of the stomach, the expression method is considerably employed, but in certain pathologic conditions, especially when the fluid is deficient, it is very often a failure, even when the stomach contains little fluid, for example, in cases of marked atony. In cases of ulcer, there is possible danger of damaging the mucus of the stomach when it is carried out irrespective of the pathologic conditions of the organ. Very frequently we meet with cases of ulcer, in which there is no special evidence pointing to ulcer. Sometimes the clinical significance is quite latent and the recent bleeding may be frequently overlooked. Therefore it is an important fact to obtain the stomach contents with the utmost care in every case, by means of the safest and the most exact method. By this apparatus the operation can be carried out very quickly and successfully in every case, with less chance of damaging the mucus of the stomach.

2. The aspiration of gas or gases in the stomach. Close the cock *U'*, and connect the pipes *F* and *G* by means of a piece of glass tubing. After filling the vessels *C* and *D* with water, close *F'* and *G'*, and connect *P* and the stomach tube *S*. Then the tube will be introduced in the stomach and the cock *H'* opened. With the lowering of the water level in the vessel *D*, the gas in the stomach will be collected in the vessel *D*. When the vessel *D* is filled with gas, the cock *H'* should be closed and the cock *F'* opened. Then the gas will be obtained in the vessels *C* and *D*. The volume of the gas under the normal atmospheric pressure may be estimated by the following two ways:

(A) Supposing that

X = The volume of the stomach gas under the normal atmospheric pressure *D*.

V = The volume of the stomach gas under the negative pressure *P*. Then we have the following equation.

$$DX = PV \qquad \therefore \quad X = \frac{VP}{D}$$

(B) After we take the stomach gas in the closed vessel *D*, the joint pipe *P* should be closed and the pipes *G* and *H* connected by means of a piece of glass tubing.

By opening the cocks G' and H' the water in the open vessel B will run down in the vessel D, and the pressure in the vessel D will gradually increase. At the instant when the pressure in the vessel D is equal to that of the external atmospheric pressure, the cocks G' and H' should be immediately closed. Then the volume of the stomach gas under the external atmospheric pressure may be read by the scale of the vessel D.

3. Volumetric measurement of the gas in the stomach. In this operation the stomach gas will be aspired in the closed vessels C and D, containing no water. Only by the lowering of the water level in the vessel A the amount of the stomach gas may be measured by the following two ways.

Before the operation, the joint pipe P and the stomach tube S should be connected. After we introduce the tube in the stomach, the cock K' should be opened. A negative pressure will be produced in the closed vessels C and D.

(A) Suppose

X = The volume of the stomach gas under the normal pressure D.

V = The volume of the air in the vessel (C and D) and pipes, connected with the vessels, under the normal pressure D.

V' = The volume of water, run out through the discharge pipe K.

We have the following equation.

$$(V+V')P = (V+X)D$$
$$PV+PV' = DV+DX$$
$$X = \frac{P}{D}(V+V') - V$$

(B) After the stomach gas is all taken in the closed vessel D, the cock K' and the joint pipe P should be closed. Then connect the pipes G and H, and open the cocks G' and H'.

The water in the vessel B will run down in the vessel D, and the low pressure in the vessel D will gradually become normal. The quantity of the water to change the negative pressure P to the normal atmospheric pressure D can be readily read by the scale of the vessel D.

Supposing

V = The volume of the air in the vessels (C and D) and pipes, connected with the vessels.

V' = The volume of the water to produce the negative pressure P in the closed vessel D.

V'' = The volume of the water to change the negative pressure P to the normal atmospheric pressure D.

X = The volume of the stomach gas under the normal atmospheric pressure D.

According to the law of Mariott we have the following equation:

$$X+V = V+V'-V'' \qquad X = V'-V''$$

In the first place it will be necessary to give a description of the construction

4. Estimation of the capacity of the stomach. Connect the joint pipe P and the stomach tube S; introduce the tube in the stomach; connect G and F. Close th cock U'; open the cocks G' and F', the water in the open vessel B will run down into the closed vessel C, going further into the vessel D, in case vessel C is full

of water, through the pipe *M*. Thus the air in the closed vessels *C* and *D* will be forced into the stomach, and the stomach will be distended. The resulting pressure in the stomach may be read by the manometer, and the volume of the air, forced into the stomach, by the scale of the blood vessels *C* and *D*. From the relation of the quantity of the air, forced into the stomach and the resulting intragastric pressure we can estimate the capacity of the stomach very easily and correctly. Preceding the maximum distention of the stomach, a gradual increase of the intragastric pressure will be noted in cases of normal muscular tone of the stomach. In cases of atony the pressure increase, preceding the maximum distention, lasts a short time, or is not so considerable as in cases of the normal muscular tone. Therefore a careful observation of the variation of the intragastric pressure will afford a significance for the diagnosis of atony of the stomach.

There are two methods of gas inflation of the stomach, namely, air inflation and carbonic acid inflation. The former is to distend the stomach by pumping the air in the stomach by means of a double bulb, after the introduction of the tube into the stomach. The latter consists in administering internally tartaric acid and sodium bicarbonate to produce the gas in the stomach. These two inflation methods are employed to render the stomach visible to inspection for the diagnosis of the dilatation or gastroptosis. But at times there may be escape of gas or air through pylorus and a distention of the intestines may occur, which may be a hindrance for the determination of the margin or the position of the stomach. It would be more difficult or impossible to get correct findings, when there is an ascites or tympanites of marked degree. By using the new apparatus for the examination, the capacity of the stomach could be estimated far more exactly and quickly than by the inflation methods, by reading the variation of the intragastric pressure, though there may be a slight escape of gas through pylorus, and neither ascites nor tympanites would be an obstacle for the examination. This new method will also tell the degree of the extragastric pressure upon the stomach, which is caused by the ascites or the gas in the intestines.

5. Lavage. Introduce the tube in the stomach, and connect the pipe *G* and the T-shape. By opening the cock *G′* the lotion in the open vessel *B* will run down in the elevating vessel *J*. When one elevates funnel *J* higher than the patient, the lotion in the funnel will enter the stomach of the patient through the stomach tube. Before the funnel is empty, one quickly lowers it below the level of the stomach to allow the washings to siphon out into a receptable. As soon as the lotion all runs out, the cock *G′* should be opened, to make the lotion run down to the funnel, as before. Thus, repeating the procedure the lavage can be quickly performed, without the trouble of pouring the lotion by the hand of the operator. This procedure should be repeated until the return becomes quite clear. When the lavage is over, one should separate the pipe *N* and the stomach tube and connect the stomach tube with the joint pipe *P*. By opening the cock *K′* the remnant of the lotion in the stomach can be completely sucked up in the vessel *D*. Thus the patient will feel no discomfort in the stomach after lavage, which may be caused very often by the remnant of the lotion in the stomach. Patients who are accustomed to lavage can perform it very easily without any assistance.

In practice there will arise at times an emergency, by which a simpler and transportable form of this apparatus is necessary. For this purpose, I have de-

signed one, based upon the same hydraulic principle. This apparatus can be operated by the bed of the patient, with very little assistance from others. One who understands the principle and the procedure of the original apparatus could employ this simple one in any operation. Further remarks and description about it would be perhaps unnecessary, but I will mention here, in addition, some remarks for the sake of better understanding.

The vessels *B* and *D* are arranged in a case, as Fig. 2 shows. The closed vessel *A*, having a capacity of about 600 c.c., is provided at the upper part with a bent pipe *C*, connected with pipe *F*, which is divided into two branches *R* and *V*. The branch *R* is attached to the air gauge *E* and the other branch *V* connected

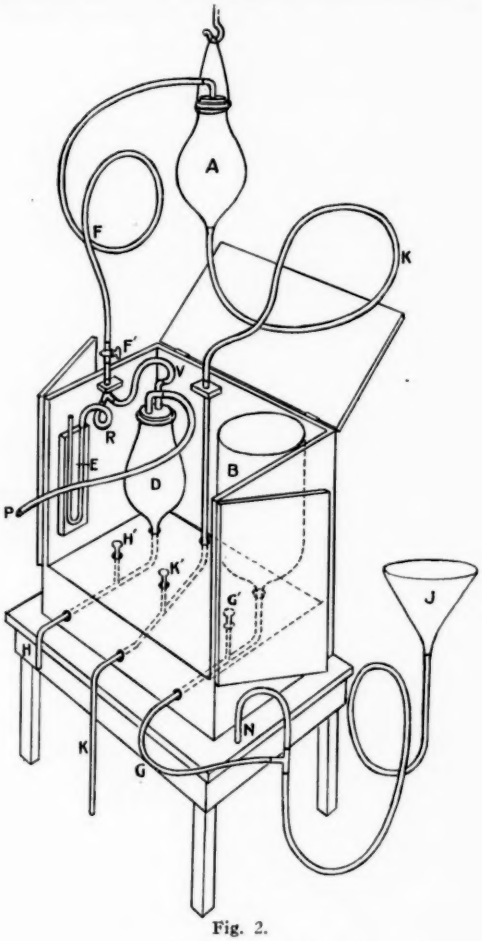

Fig. 2.

with the closed vessel *D*. The vessel *A* is fitted at the lower part with the discharge pipe *K* with a cock *K'*. The closed vessel *D* is fitted at the upper part with a joint pipe *P*. The upper part *M* of the vessel *D* is closed with a rubber stopper.

The open vessel *B*, having a capacity of about 4000 c.c., is provided at the lower part with a discharge pipe *G* with a cock *G'*, which communicates with a connecting tube *N*, attached to a funnel *J*.

This apparatus can be operated in the same manner, mentioned already. Before any operation the following points should be noted. Close *H′*, *K′*, *G′*.

The vessel *A* should be filled with fresh water, the vessel *B* with a suitable lotion. Close the upper part of the vessel *A*, open the cock *F′*. One can hold the vessel *A* in any height to produce a suitable pressure, because the air pressure in the vessel *D* depends upon the height of the water level of the vessel *A*.

1. The aspiration of the gastric contents. Connect the pipe *P* and the tube in the mouth. Open the cock *K′*.

With the lowering of the water level in the closed vessel *A*, the air pressure in the closed vessel *D* would be reduced, which is shown by the air gauge *E*. The gastric fluid can be sucked up completely in the closed vessel *D*.

2. The aspiration of the gas or gases in the stomach. Fill the vessel *D* with water. Close the cock *F′*, connect the pipe *P* with the tube in the mouth. Open the cock *H′*.

With the lowering of the water level in the vessel *D* the gas or gases in the stomach will be sucked up in the vessel *D*. According to the same means, mentioned above, the volume of the stomach gas can be estimated.

3. Volumetric measurement of the gas in the stomach. Connect the joint pipe *P* with the tube in the mouth. Open the cock *K′*.

With the lowering of the water level in the vessel *A* a negative pressure will be produced in the vessel *D* and the gas or gases in the stomach will be forced in the vessel *D*. After the same way which I have mentioned already, the volume of the stomach gas can be estimated.

4. Estimation of the stomach capacity. Connect the joint pipe *P* with the tube in the mouth. Fill the vessel *A* with water. Open the upper part of the vessel *A*. Close the cock *F′*

When we open the cock *K′*, after connecting pipes *H* and *K*, the water in the vessel *A* will run down to the vessel *D* and the air in the vessel *D* will be forced into the stomach. The air gauge will show the variation of the pressure in the closed vessel *D*, which is equal to that of the intragastric pressure.

5. Lavage. The lotion should be poured into the open vessel *B*. Connect the pipe *N* with the tube in the mouth. Open the cock *G′*. When we hold the funnel below the position of the patient, the lotion will run down to it. By elevating the funnel, the content in it will run down in the stomach, the washings flowing out of the stomach again when the funnel is lowered below the patient's stomach. The procedure will be repeated until the gastric fluid returns clear. After lavage the pipe *P* and the tube should be connected. By opening the cock *K′* the remnant of the washings in the stomach can be sucked up in the vessel *D*.

PREFORMED AMMONIA IN THE SPINAL FLUID*

By P. F. Morse, M.D., and E.S. Crump, M.D., Detroit, Mich.

THE determination of the various nitrogen partitions in the spinal fluid for clinical purposes seems to have been largely neglected. Kahn[1] showed that with certain modifications Folin's direct Nesslerization methods were applicable to the spinal fluid, and gives tables showing the value of the various partitions. He found the total nitrogen to be 17.5 mg. to 31.25 mg., the nonprotein nitrogen 14.0 to 33.63 mg., and the urea nitrogen 6.31 to 21.62 mg. per 100 c.c. of spinal fluid. The wide variation in each of these series is interesting and the fact that the nonprotein nitrogen of one series slightly exceeds the highest total nitrogen value in the other makes the wide variation all the more apparent. Two years ago we tried the direct Nesslerization of spinal fluid by adding Nessler's reagent directly to the fresh spinal fluid and noting the depth of brown color which developed. We satisfied ourselves that in cases of acidosis and uremia the preformed ammonia was increased. On account of difficulties with the technic Nessler's solution was given up for the time for nitrogen determinations and the Kjeldahl method resumed for blood work. No more spinal fluids were tested until Folin's[2] new system for blood analysis was published, when direct Nesslerization methods were again resumed with satisfying results. No doubt a complete study of spinal fluid nitrogen partitions would be of clinical value, and we have carried this far enough to find that these determinations can be made with great simplicity using the reagents employed in the system of Folin referred to above. Kahn believed that the calcium present in the spinal fluid prevented successful Nesslerization and added alkali and filtered to prevent this. We find it much simpler to add a small crystal of potassium oxalate and centrifugate after solution has taken place. The total nitrogen can then be determined very simply, using 2 c.c. of spinal fluid and one c.c. of the sulphuric phosphoric digestion mixture.

At this time we wish to present an extremely simple method for the determination of excess preformed ammonia in the spinal fluid. As far as we have gone this increase has run parallel to blood nitrogen retention wherever the latter could be determined, and we have found this simple test to be of great value for quickly determining the cause of coma. After a little practice a close approximation of the blood nitrogen can be estimated from the depth of color developed.

The test is performed as follows:

To an appropriate quantity (2 c.c.) of spinal fluid, an equal quantity of Nessler's reagent is added. In normal persons and in conditions not tending to acidosis or nitrogen retention, scarcely any brown color develops. A cloudy greenish gray precipitate gradually forms and the fluid turns a dirty pale green color. When there is acidosis or nitrogen retention from

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CASE	ALBUMIN IN URINE	BLOOD PRESSURE	CELL COUNT	GLOB.	SPINAL FLUID WASS.	BLOOD NON-COAG. N.	CLIN. DIAG.	NESSLERIZATION OF SPINAL FLUID
1						98	Uremia: Prostatic Hypertrophy	++++
2						30	Cerebrospinal Lues	neg.
3						32	Normal person	neg.
4						75	Chr. Nephritis, Uremia	++++
5						38	Brain abscess	neg.
6	+++	230	1	neg.	neg.	63	Chr. Nephritis with hypertension	++++
7			20	+	++++		Cerebrospinal Lues	neg.
8						35	Subacute Pancreatitis with exacerbations	+
9			700	+			Mastoiditis with brain abscess.	±
10			450	+			"	neg.
11			Pus	+			10 hours before death	+
12	++++	160				35	Chr. focal Nephritis	±
13			6	+	++		Cerebrospinal Lues (?)	neg.
14		118	370	+	neg.		Otitis Media Brain abscess	neg.
15	++++		Pus	+			Pneumococcus Purulent Encephalitis. Rt. convexity following frontal sinusitis. Autopsy	neg.
16			4	+	blood		Syphilis, Brain (Gumma) Autopsy	neg.
17			18		+++	60	Tabes Dorsalis	+++
18								+++
19			16	+	+++		Cerebrospinal Lues	neg.
20			40	+	+++		General Paresis	neg.
21			10	+	+++		Cerebrospinal Lues	neg.
22			6	neg.			?	neg.
23	neg.	148	3	neg.	blood ++++ S. F. neg.		Syph. Endarteritis	neg.
24			40	+			Tabes with Gastric Crisis	neg.
25					neg.		Gastric Ulcer	neg.
26							Non-Syph. Chorioretinitis	neg.
27								++++

any cause, a deep brown color develops immediately, the depth of color depending upon the amount of ammonia present in the spinal fluid. Only one precaution is necessary. The fluid must be free from contaminating bacteria. These form ammonia and give false readings. Sterile spinal fluids well corked give good reactions even when several days old. The reaction is read immediately (within thirty seconds). In general, cases of acidosis associated with infection, and terminal stages of meningitis, develop less color than cases of uremia with nitrogen retention.

We have tried several substances for standard tubes to assist in reading the reaction. Appropriate mixture of Bismark brown with triple strength Lugol's solution will give a color which exactly matches Nesslerized nitrogen standards even in the Duboscq colorimeter. The color gradually fades, however. Tubes of different strength picramic acid can be used for rough comparison as pointed out by Egerer and Ford.[3] Inasmuch as a considerable cloudiness develops upon the addition of Nessler's reagent to spinal fluid, we think that for practical clinical purposes standards are not necessary, and we estimate the depth of color reading from negative to four-plus. The table which follows shows the results in 28 consecutive examinations. The data was taken from the routine laboratory card and is not always complete in all details.

The accompanying table requires no analysis to show that cases of nitrogen retention give a strong reaction for ammonia in the spinal fluid. Cases 1, 4, 6, and 17 demonstrate this. Cases included with a bracket are successive examinations on different spinal fluid samples from the same patient. Samples 9, 10, and 11 are from a child with brain abscess and general meningitis from a mastoid, in whom a certain degree of acidosis presumably developed. The weak reaction given by No. 8. was also due to acidosis. The specimen was removed when the patient was unconscious and having a convulsion. Recurrent attacks of vomiting followed by unconsciousness and convulsions associated with deep jaundice occurred intermittently over a period of two weeks after a gall bladder drainage. The patient finally recovered completely.

The case from which specimens 17 and 18 were removed is especially instructive. No kidney insufficiency had been detected. The man had all the signs and symptoms of tabes, including a Charcot joint. After we obtained a strong ammonia reaction on two different occasions, the blood nitrogen examination was made with the result that 60 mg. per 100 c.c. was found. The ammonia increase in the spinal fluid and the nitrogen retention thus pointed to the additional factor of kidney insufficiency. Specimen 27 was a spinal fluid from an unknown source which had been allowed to stand around the laboratory until heavily contaminated by bacterial growth. The ammonia reaction obtained was probably due to this. Case 12 with a heavy urinary albumin and a blood pressure of 160 shows a blood nitrogen of 35 and a doubtful spinal fluid ammonia reaction. These findings are correlated and are common in acute exacerbations of focal nephritis where parts of the kidney are acutely affected, leading to the urinary findings of

nephritis without clinical or laboratory evidence of nitrogen retention or, in other words of lowered kidney function. In these cases there is enough normal or functionally normal kidney parenchyma still left to carry on the function.

The Nessler's solution which we use is made according to Folin's[1] directions as follows: "Transfer 150 gm. of potassium iodide and 110 gm. iodine to a 500 c.c. Florence flask with 100 c.c. of water and an excess of metallic mercury (140-150 gm.) Shake the flask continuously and vigorously for 7 to 15 minutes or until the dissolved iodine has nearly disappeared. The solution becomes quite hot. When the red iodine solution has begun to become visibly pale, though still red, cool in running water and continue the shaking until the reddish color of the iodine has been replaced by the greenish color of the double iodide. This whole operation does not take more than 15 minutes. Now separate the surplus mercury by decantation and washing with liberal quantities of distilled water. Dilute the solution and washings to a volume of two liters. If cooling is begun in time, the resulting reagent is clear enough for immediate dilution with 10 per cent alkali and water and the finished solution can at once be used for Nesslerizations."

For use 75 c.c. of the above stock solution are added to 75 c.c. of water and 350 c.c. of 10 per cent NaOH. The NaOH must vary but little from 10 per cent. We make up a 60 per cent solution of NaOH as Folin advises, allow the sediment to settle out and pipette off the supernatant fluid and dilute it to 10 per cent. It must be titrated against standard acid and the strength adjusted to exactly 10 per cent if it is to be used for the nitrogen determinations according to Folin's method.

We report this simple laboratory test at this time because it can be done so easily and quickly by anyone without special apparatus and with reagents obtainable anywhere. Complete data regarding all the nitrogen partitions in the spinal fluid might add still more clinical information, but this simple test for preformed ammonia in the spinal fluid we have found clinically helpful. We have not yet had an opportunity to test the reaction in diabetic coma.

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EDITORIALS

Bilharziasis in the Light of Modern Experimental Treatment With Antimonial Compounds

SINCE the days when "Mineptah's soul, like a bird, suddenly flew up to heaven to exist forever in the bark of the sun," thereby entrusting the salvation of ancient Egypt to his distinguished son Rameses II, the humble servants of the Pharaohs and their successors have suffered from an ailment known as the ĀĀĀ disease. This affliction Phister[1] has supposed was none other than that of Bilharziasis, whose true etiology remained a mystery from the time of Rameses (and perhaps very much earlier) until it was finally worked out in the year 1852. Thus, now for over half a century the true exciting organism of this disease, i. e., the Schistosoma hematobium (Bilharz) has been well known. But notwithstanding the prolonged period during which man has suffered from this tropical, or semi-tropical, disease, many of the most fundamental questions regarding it have been answered only in the most recent times, or else still remain unanswered.

The parasite which causes bilharziasis belongs to the extensive group of organisms known as trematodes, or fluke worms. The fluke worms are usu-

ally flattened organisms, somewhat tongue-shaped, and provided with powerful suckers and occasionally hooklets. In man there are four different clinical classes of trematode diseases (distomatosis, distomiasis) which may be regarded as typical, in the sense that in these four instances the infection of man by certain trematodes is more or less normal in the life cycle of the parasite under consideration. These cases include (1) pulmonary distomiasis, with cerebral or other infection as secondary; (2) hepatic distomiasis, with splenic or intestinal infection as secondary; (3) intestinal distomiasis, and (4) a venal distomiasis, while in a few rare instances (5) an ophthalmic distomiasis, which may be an accidental secondary form of hepatic distomatosis, has been described.

A point of very marked interest in reference to recent discoveries, is the fact that the parasites in question, *except the blood flukes* (which cause bilharziasis) are hermaphrodites. The life cycle of the trematodes is quite complicated and may involve one or more generations which live outside of man. The parasites may require an intermediate host, or in some cases, direct infection may perhaps occur. Blood fluke disease in man may be due to either of two distinct organisms, the African blood fluke (Schistosoma hematobium or S. mansoni) or the Asiatic blood fluke (S. japonicum). The latter organism, which has been known only since 1904, is found in Japan, China, and the Philippines. The African blood fluke is found chiefly in Africa and the adjacent islands, but extends to Persia, Arabia, India, rarely to Panama, Cuba and Porto Rico and occasionally elsewhere, including the United States.

The sexes are distinct in these blood flukes, but the female, which is longer but much smaller in diameter than the male, is carried in a gynecophorous groove running along the ventral surface of the male. The eggs of the African fluke are oval, 135 to 160μ long by 55 to 66μ broad and are provided with a terminal (Bilharzia hematobia) or lateral, subterminal (Bilharzia mansoni) spine, but not with an operculum. The eggs of the S. japonicum are 60 to 90 by 30 to 50μ, and are not provided with the terminal or subterminal spine, nor with an operculum. The young S. hematobium and mansoni worms live in the veins of the liver; in the portal vein there are but few young paired individuals, but in the veins of the intestine and bladder wall paired flukes are numerous. Oviposition begins while the parasites wander from the portal vein to the pelvis, and eggs are deposited in various organs. The ova increase in size as they work their way through the tissue, into the lumen of the intestine or bladder. During this process a ciliated embryo (miracidium) is developed, and this organism escapes from the egg shell when it comes into water. But the eggs apparently do not hatch out so long as they remain in undiluted urine. In 1915 Leiper[2] worked out the complete cycle of development and life history of the bilharzial worms. He found the noneyed, bifid-tailed cercariæ characteristic of the genus in two genera of snails, Bullinus contortus and Planorbis boissyi. These snails were shown to harbor two different species—Bilharzia hematobia (terminal spined ova) and Bilharzia mansoni (lateral spined ova). Recently Fairley[3] has demonstrated that bilharzial parasites and their ova exert a deleterious influence on the tissues of their definite host, man, mainly by the production of toxins, and not merely mechanically. These toxins call into

action cellulo-humeral responses which neutralize or limit their activity. As a result immune bodies, including complement-fixing substances, are produced, and a complement-fixation test for bilharziasis has accordingly been devised by Fairley.[3] As antigen an alcoholic extract of the infected livers of snails (P. boissyi) was employed. Positive complement-fixation was obtained in a high percentage of cases in man as well as in experimentally infected monkeys. The practical application of this test, Fairley considers, will facilitate the diagnosis of bilharziasis in the early stages of the disease before localizing symptoms have developed, and also in estimating the effect of the intravenous administration of drugs on the adult parasites.

It has long been supposed that the clinical symptoms of the disease are not due so much to the presence of the adult worms as to that of their ova which are liable to obstruct vessels and give rise to important pathologic developments. Lodged, for example, in the small veins of the vesical plexus, an inflammation of the bladder and rupture of the occluded vessel with the appearance of blood in the urine are apt to result; or if in the wall of the lower bowel, proctitis or colitis with dysenteric hemorrhages. The vesical symptoms are not infrequently marked, pain and tenderness in the hypogastrium, a burning pain in the urethra, especially on micturition, difficulty of micturition, sometimes evidence of prostatic swelling, with urine containing blood, pus and mucus as well as the ova of the parasite. Sometimes the inflammatory disturbances may extend along the ureter to the pelvis of the kidney and the latter organ itself, inducing the symptoms of a more or less grave nephritis. Occasionally from passage of the ova into the liver or lungs symptoms referable to these organs may also be met. Fatal results are to be apprehended after a variable period of such symptoms, with secondary anemia, debility and exhaustion.

In Japan and China the Schistosoma japonicum has been met in cats and in man, and has been believed to be responsible for an endemic affection known in Japan as Katayama, which is characterized by enlargement of the liver and spleen, disturbances of the appetite, diarrhea (the dejecta often containing blood and mucus), and in severe cases anemia, fever, ascites, and edemas, and occasionally death from exhaustion. The parasite inhabits especially the arterial side of the portal system. It is somewhat smaller than the African fluke, and the male is distinguished by his nontuberculated integument. The ovum has no spine, is regularly oval, perfectly smooth, and with a much thinner shell. The ova are deposited mainly in the mucosa and submucosa of the large and small intestine, especially the former. From here they escape with the feces. The life history of these flukes outside the human body is still obscure.

Notwithstanding the prolonged lapse of centuries during which man has suffered from bilharziasis, still nothing but palliative treatment has been known until the present time. The story of the recent accomplishments in the management of the African blood fluke disease constitutes one of the brightest pages in the history of medicine. In 1918 Christopherson[4] introduced the use of tartar emetic by intravenous injection for the treatment of these patients. He was led to try this form of medication by reason of the encouraging results which had followed the use of antimonyl tartrate in such diseases as oriental

sore, internal leishmaniasis and naso-oral leishmaniasis (espundia) as found in the Sudan.

The method used by Christopherson consisted in giving a course of injections on alternate days for a period of 15 to 30 days, commencing with ½ grain dissolved in 6 mils of distilled water and increasing by ½ grain up to 2 grains and continuing this dosage until a total of 25 or 30 grains had been given. This amount Christopherson considers to be the required killing dose, notwithstanding that all the symptoms of the disease often completely disappear after the first few injections. This method was introduced by Christopherson at the Khartoum Hospital in May, 1917, and was found to be equally effective in curing both rectal and vesical cases. By September, 1918, he had treated 13 cases of the disease with apparently complete cure in all instances, but with relapse in from one to eight months in three cases. As a result of his experiences he considered that potassium antimonyl tartrate is a definite cure for bilharziasis, and that the intravenous injection of the drug kills the Schistosomum hematobium in the blood and tissues and renders it harmless. If the dosage be too small to completely destroy all the organisms, still their activities will be suspended or considerably interfered with. As a matter of interest here it may be noted that McDonough has reported that he had made some use of tartar emetic before Christopherson published his experiments, and Major Strong of the Australian Medical Service with one or two of his colleagues had also used tartar emetic in small doses at week intervals as early as 1916. But no one felt convinced of the possibility of curing the disease, nor had any one the courage to adopt the truly heroic dosage which is necessary to affect the bilharzia worm and its ovum.

In order to follow the course and rapidity of the drug's action in curing the disease, Innes[5] has studied the change in the length of time required for ova which have been freshly passed in the urine to hatch out when the urine is diluted with water. Thus in one case before treatment ova (which were numerous in the urine) hatched out in ten minutes on the addition of water. On Nov. 5, one-half grain of tartar emetic was given, on Nov. 7, one grain, on Nov. 9, one and one-half grains and on Nov. 11, two grains. On these last two days the ova hatched in 15 minutes. Thereafter 2 grains were given every second day until Nov. 27. On Nov. 13 the ova hatched in half an hour; on Nov. 15 in one hour; on Nov. 17 in one and one-fourth hours; on Nov. 19 the ova hatched, but movements were very sluggish; on Nov. 21 the ova did not hatch in three hours, as was true also on Nov. 23. On Nov. 25 there were a few ova, and on Nov. 27 none. The patient was discharged on Nov. 28. When examined again on Jan. 12, 1919, the urine was quite clear, but contained a few black ova, which did not hatch. This case also illustrates another point which has been emphasized by Christopherson,[6] namely, that dead ova may be discharged by a patient for many months (up to two years) after the parent worms may be considered to be dead (that is, after completion of the course of injections).

That the embryos in the tissues are attacked and killed is a matter of the greatest importance, for thus the patient ceases to be a carrier of the disease and the ova discharged can no longer infect the various species of fresh water

molluscs (such as Bullinus dybowski, B. innesi, B. contortus and Planorbus boissyi) which act as intermediate hosts for bilharziasis in Egypt. The fact that antimony given to a bilharzia patient kills the parent worms in the patient means benefit to one human being, but the fact that antimony also sterilizes the ova which have been deposited by the parent worms before death in the bladder and rectum, renders the effect of antimony a hundred fold greater, for the benefit extends possibly to hundreds who might be infected by the patient, and this goes on all the time the ova are being eliminated. Thus a direct frontal attack on bilharzia as an endemic disease is possible, and it seems probable that by this prophylactic action of the drug, bilharzia may be practically banished from such countries as Egypt.

The dangers attendant upon the administration of such large quantities of antimony are by no means to be underestimated, and fatal results[7] in connection with the use of the drug have already been reported. The double salt [$K(SbO)C_4H_4O_6$] is not readily dissociated, and it is therefore much less corrosive than the antimony chloride. Other compounds of antimony will in all probability be found to be useful in the disease, and by analogy with the complex organic compounds of the closely related arsenic, we may expect that some of these bodies may be more effective, and in all probability, much safer than tartar emetic itself. Already Caronia[8] as early as 1916, experimenting with antimonyl preparations in external kala-azar and leishmaniasis, has employed acetyl-p-aminophenyl stibiate of sodium which he preferred on account of its greater efficacy, easy absorption and less toxicity. And Sir Leonard Rogers[9] has used colloid antimony sulphide and sodium antimonyl tartrate.

Toxic symptoms[10] following the injection of the drug are very common but usually not serious. Among these may be mentioned cough and pharyngeal irritation, stiffness of the neck and shoulder muscles, nausea, vomiting, diarrhea, headache, pyrexia, vertigo, body pains, general pruritus and loss of weight. In some cases, of course, if the extent of the treatment has been insufficient there will be a relapse with hematuria, etc. Of the complications resulting from the injections themselves one may get a marked depression with vertigo, weakness, coughing, dyspnea, etc., if the solution is injected too rapidly. Phlebitis may occur in the injected vein, and if any of the solution escapes into the surrounding tissues a severe, inflammatory reaction with probable necrosis and sloughing is prone to be produced. This reaction is much more severe than usually occurs under similar circumstances with arsphenamine. This has, of course, long been known as the result of injections of antimony in trypanosomiasis, etc.

In cases in which the treatment is too intensive or prolonged, there is the constant danger that symptoms of chronic antimony poisoning may occur. In ordinary circumstances cases of chronic poisoning with antimony are rare and difficult to diagnose. Headache, giddiness, drowsiness, confusion and indistinct sight appear, and the patient complains of anorexia, heaviness, discomfort or pain in the stomach region, and diarrhea is liable to be marked. Pustular eruptions may develop, and general weakness, albuminuria, exhaustion and final collapse mark the severer stages of the intoxication. Albuminuria in a patient, unless caused by the disease, therefore, demands caution in the administration of

the drug. When taken by stomach the minimum fatal dose of tartar emetic is very variable, as the greater amount of the substance is usually removed by vomiting. Recovery has occurred after very large quantities, but in other instances one-tenth of a gram (2 grains) has caused death. Acute poisoning with antimony resembles very closely that produced by arsenic and is characterized by excessive perspiration, salivation, nausea and vomiting, profuse, watery diarrhea, great muscular weakness, and finally collapse. When large quantities are injected intravenously or subcutaneously vomiting and purging occur because the metal is excreted into the stomach and intestines and here acts as a severe local irritant. In chronic poisoning there may be ulceration in the small intestine, especially around the lymphatic follicles and Peyer's patches, and extensive fatty infiltration of the internal organs occurs. In an animal with chronic antimony poisoning we have seen an intense icterus which permeated every tissue of the body. This was perhaps largely secondary to fatty infiltration of the liver.

Regarding prophylaxis against bilharzia Elgood and Cherry[11] have made some interesting suggestions. These authors believe that infection generally occurs from coming in contact with, or using the water contained in the small irrigating channels in the fields, or in small pools, and not as a rule, from the large open canals or from the Nile itself. The reason for this seems to be that the snails from which the cercariæ are derived are found in great numbers along the small water channels or pools, but are much less often found along the larger bodies of water. And the authors suggest that destruction of these snails by ducks, such as the Pekin, Muscovy or Indian Runner might be of great assistance in limiting the spread of the disease. And by way of experimentation this means of destroying the snails might first be tried out on a small scale by supplying a good number of ducks to a limited section all of which was supplied by water derived from a single small canal and its branches.

As mentioned above trematode infections are due to a variety of different organisms, and in view of the splendid results obtained with tartar emetic in the case of the African blood fluke disease, the question naturally arises as to whether or not antimony compounds might be used in other fluke infections also. But as pointed out above, all these other trematodes are hermaphroditic except the blood flukes. It will be a matter of interest to see what the later history of these other varieties of distoma infections may be.

In conclusion it is interesting to note that antimony has long borne a most vacillating reputation in the history of medicine. Raised to great prominence in the 16th century by Paracelsus, in 1604 John Thölde, who wrote under the pseudonym of the mythical fifteenth century monk, Basil Valentine, published his "Triumphant Chariot of Antimony," which popularized the metal with the medical profession for centuries. Tartar emetic was first described by Adrian Mynsicht in 1631, and in 1657 Louis XIV was cured of typhoid fever by antimony. Notwithstanding numerous deaths produced both accidentally and otherwise by the administration of antimony, John Huxham was able in 1755 to win the Copley medal for his essay on antimony. At one period graduates in medicine of the University of Heidelberg were required to take an oath never to use

it, because of the injury which its very extensive employment was believed to cause. In recent years, at Cushny's suggestion, various investigators have used injections of antimony-sodium tartrate successfully in the treatment of experimental and human trypanosomiasis. And the latest use of antimony as applied to the treatment of bilharziasis bids fair to be the most lasting of all.

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—*D. E. J.*

*The Spread of Bacterial Infection**

TOPLEY treats this broad, interesting, and important subject in the Goulstonian Lectures for the current year. He starts out by saying: "The subject may be approached from at least three sides, the epidemiological, the bacteriological and the biometrical. The first and the third may perhaps be regarded as identical, but the statistics of the epidemiologist, who is concerned mainly with the historical and geographical aspects of his subject, differ so widely from those mathematical methods more recently evolved that biometrics has developed a technic which it seems better to regard as belonging to a separate branch of biological science. While it is with the bacteriological aspect of the question that I am here mainly concerned, yet it is impossible to consider one side of the problem alone without losing all sense of proportion."

There are, so far as we know no new epidemic diseases. All have afflicted mankind through all historical time. They flare up, manifest great activity, and then subside and may apparently at least, wholly disappear from wide geographical areas for variable periods of time. An explanation of why the specific virus remains dormant for certain periods and when and how it exists during these periods is highly desirable, as is also a knowledge of the stimuli which awaken it into renewed activity. So far as we know no disease-inducing virus can continue to multiply and live, at least through generations on inorganic matter. A few, like the plague bacillus, may thrive on certain lower animals, but there is no evidence that this is true of the causal agents of most infectious diseases. Even in those diseases common to man and beast, like tuberculosis, the strains

*Lancet, July 5, 12-19, 1919.

have been confined to the animal species so long and so continuously that they have acquired characteristics sufficiently marked to render their differentiation easy and certain.

Topley is inclined to conclude that during the interepidemic period the virus continues its existence as a harmless parasite in man. He says: "The first difficulty with which we were faced in forming any theory of the spread of bacterial infection, which should conform to the known facts of epidemiology, was to find some explanation of the perpetuation of the virus during interepidemic periods. The bacteriological data which have accumulated, especially during the last twenty years, have shown that the causative agents of specific diseases are to be found in apparently normal persons who give no history of having been in contact with the disease in question as well as in contact with actual cases of the disease. Moreover, the organisms in question have been shown, in certain cases, to persist for long periods of time in or upon the tissues of their hosts, and we must always remember that the difficulty of bacteriologic technic is likely to lead to a serious underestimate. Clinical and epidemiological investigations have yielded confirmatory evidence, and we are thus left with a conception of the virus of a given disease being distributed fairly widely throughout the world as an apparently harmless parasite on the human host, but taking on during epidemic periods a new and sinister role, only to relapse again into comparative quiescence as the epidemic subsides."

He explains the rise of the epidemic wave as follows: "There are at least three possible explanations—an increase in the power of the parasite to produce disease, a decrease in the resistance of the host, and some attraction in the surrounding circumstances which favor the transference of parasites from case to case without any alteration of the pathogenicity of the one or in the resistance of the other. The third of these hypotheses may, I think, be disregarded. That alterations in environment may be the determining cause in initiating an outbreak of bacterial disease is probable enough; but they will almost certainly act through the variations which they bring about in the other two factors. The whole of bacteriological knowledge is clearly against the occurrence of a considerable epidemic in which the pathogenicity of the parasite and the resistance of the host remain constant. Again, while we may well believe a lowered resistance of a certain number of the host-species to be an important factor in the initiation of the process, yet we can not believe that it is the whole story. The widespread ravages of many epidemics would seem altogether to preclude such an explanation. We seem forced therefore to the conclusion that an increase in the pathogenicity of the specific parasite is an essential factor in the rise of epidemics, excluding from this category small sporadic outbreaks which may be due to the introduction of a fully virulent parasite by a healthy carrier in some other way."

In regard to the decline of the epidemic, Topley thinks that this may be due to a decrease in the virulence of the bacterium, increased resistance of the host or to changed environmental conditions, resulting in lessened opportunities for the transference of the parasite. He rejects the possibility of the termination of an epidemic by the exhaustion of susceptible material. On this point we

wish to dissent. That epidemics of measles and mumps are often terminated only by the exhaustion of susceptible material we believe to be fully demonstrated by experience with those infections in some of our camps. The history of measles at Camp Wheeler seems to be best explained in this way; in fact, no other explanation occurs to us.

—*V. C. V.*

Food Poisoning

PERHAPS it is true that since the beginning of the great war the number of cases of food poisoning, especially those due to preserved and canned foods has increased. If one can judge anything from the number of serious studies in scientific journals this is probably true. If one can judge from the number of instances cited in the daily press it is certainly true. Nevertheless this truth has not been established by scientific investigation. What has happened is that investigators have turned seriously to work to determine how much infection of canned foods exists, what proportion of canned food is spoiled and the causes of the spoiling, and what the causes of the deterioration of the food are due to. Because, during the war, the amount of home canning and preserving increased tremendously, it would be of value to know the number of cases of sickness and death caused by eating home products as compared with factory products. This we do not know except by inference.

The most pretentious work on the bacteriology of canned foods is that of Weinzirl[1] who by way of introduction calls attention to the fact that the annual consumption of canned foods probably totals 250,000,000 cases. Weinzirl undertook to determine the organisms present in canned foods both in commercial and in spoiled samples. His series includes specimens of spoiled canned food, including fruits, vegetables, meat and milk; experimental packs chiefly vegetables and sardines; and commercial canned foods purchased in the market and received from packers in every part of the United States. In all 1,018 samples were studied. In spoiled and in underprocessed food spore-bearing and non-spore-bearing bacteria were found. In spoiled sardines the colon group prevailed. Swelling of fruits and vegetables is caused by yeasts and anerobic bacteria, most commonly B. welchii. In commercial canned foods microorganisms (all spore-formers) were found in 23 per cent of the samples. In no instance were members of the paratyphoid-enteritidis group found nor was B. botulinus ever isolated. In other words no food poisoning organisms were found. The conclusion from this work seems to be that the ordinary commercial canned foods are safe.

It is to be borne in mind that Weinzirl made no intensive study of putrid food, because it was presumed such food would never be consumed. This presumption is taken exception to by Thomas, Edmonson and Giltner who have made a study of a series of poisonings due to canned asparagus[2] which was definitely spoiled and which had an offensive odor. In this case the asparagus was preserved by the cold-pack method with single sterilization. Of the five persons who ate of this, four died within 36 hours. From the material B. botulinus was

isolated. The organism isolated resisted heating to 100° C. for one hour, and resisted autoclaving at 10 pounds pressure for 15 minutes. The toxin was destroyed by heating for ten minutes at 70-73° C. The organisms can live and multiply at 12° C., in foods (cheese and peas).

B. botulinus is a spore-bearing, heat-resisting anerobe, which produces a powerful toxin. Fortunately it is not a very common contaminator of food. It is one which can probably be completely eliminated from foods by careful selection of the materials to be canned and by careful attention to the canning apparatus. If the utensils are scrupulously clean, and only fresh, sound, clean fruits and vegetables are used, and treated by the best processes little if any danger will exist.

It is probably true that most cases of food poisoning are due to food which has been "set aside to be used up." In such food unless it is kept very cold, fermentation may occur with the production of toxic chemical substances (ptomaines). Opportunities for this are present always, particularly perhaps in fish. Hunter and Thomas[3] found 224 out of 530 cans of salmon to contain spores of a particular organism but found no evidence that it caused changes in the material after it was canned. Obst[4] found that anerobic spore-formers were abundant in the sardine canneries, that they were not killed by commercial process and that it was only necessary to incubate a few cans at 37° C. to obtain one or more "swells."

All these facts taken together serve to emphasize the warning to avoid spoiled food of any sort, but particularly spoiled canned food. Most canned food is perfectly safe. Any can that is "swelled" should be discarded and destroyed, and canned food, especially canned fish, should be used immediately after it is opened, and not allowed to remain for many hours before it is eaten.

But the recent cases of food poisoning that have created much excitement; i.e., the Canton, Ohio, and the Detroit, Michigan, cases were not due to home preserved food nor were they due to fish or to food left open. They followed eating canned ripe olives. In these cases not only were the disease-producing organisms found in the cans from which the food had been taken, but they were also isolated from the contents of unopened cases, and were, apparently, B. botulinus. The offending product was that produced by a single firm of manufacturers and its sale has been stopped and all possible of the stock on hand in several states has been seized and condemned. It is probable that an investigation of the factory will be undertaken.

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—*P. G. W.*

Constitutional Visceroptosis

IN CONTRAST to diseases manifested by pathology in the organs above the diaphragm and which are for the most part easily detected and diagnosed by the simpler methods of examination, pathological processes of the gastrointestinal tract are often obscure and frequently difficult of accurate diagnosis. Even renal disease has, following the application of the various functional tests, become susceptible to more accurate qualitative and quantitative determination than are some of the equally common conditions found in the abdomen. The use of the roentgen ray has aided greatly in the study of gastrointestinal disease, and particularly those conditions having as a basis of prominent symptom, either abnormal position or abnormal motor function of the abdominal viscera. The advent of detailed x-ray examination of the intestinal tract has added considerably to our knowledge of constitutional visceroptosis with its concomitant neuraesthenic and other symptoms,—a condition which the busy practitioner is called on almost daily to remedy.

This constitutional or primary condition must first be differentiated from secondary ptosis, due to weakness of the musculature of the abdominal wall. The latter is most frequently seen in women who have borne children and is evidenced by a loose, pendulous abdomen. The primary form on the other hand is often, in fact usually, found in thin individuals with flat or even scaphoid abdomen. Secondary ptosis, according to Keith and Sherrington, may depend for its existence on the absence of integrity of the reflex nervous arcs between the peritoneal nerves and the abdominal muscles. In their opinion muscle tone of the abdominal wall results from afferent stimuli from the sympathetic nervous system including the Pacinian bodies and neuromuscular terminations in the intestines. Weakness of this mesenteric plexus reflex may produce the disease. On the other hand it may be due to inherent weakness of the muscles themselves. Severing of the abdominal muscles of an upright cadaver results in a severe degree of ptosis with the external signs as described and a marked dropping of the abdominal viscera. In secondary ptosis the prolapse of the organs is due to lessened support and not to lengthening of the mesenteric and ligamentous attachments.

Primary or functional splanchnoptosis is based on a developmental abnormality, chiefly a lengthening of these attachments, and is usually associated with certain other developmental deviations. Keith describes a quasi-inflammatory process in the peritoneum that takes place normally between the third and fifth months of embryonic development and which results in fixation of the mesenteries to the tissues near the spinal column, of the ascending colon to the perirenal tissue, of the back of the cecum to the abdominal wall, and of the terminal ileum in the iliac fossa. This he considers a necessary expedient preliminary to assuming the upright posture and one which prevents later twists and kinks.

Failure of or diminished intensity of this adhesive process would result in looser peritoneal and longer ligamentous attachments. These and the frequently accompanying long, narrow chest, acute intercostal angle, and narrow

upper abdominal aperture, all combine to produce the familiar visceroptosis with prolapse of the stomach, liver, kidneys, cecum, transverse colon and colic flexures. Naturally in many instances the picture as described is not complete.

It is important to emphasize the fact that the developmental deviation is rarely, if ever, limited to this peritoneal process, but is accompanied by other more generalized changes, particularly in the skeletal form. Ansell, in classifying the various degrees and types of visceroptosis as seen by the roentgenologist, suggests that individuals be classed in four groups. These he describes as the *hypersthenic habitus,* the *sthenic,* conforming to the average or normal build, the *hyposthenic,* and finally the *asthenic* habitus.

The individual corresponding to the first type is characterized by massiveness of build, wide intercostal angle, a short, broad and deep thorax, a long abdomen with relatively narrow pelvis, and showing on roentgen examination transverse heart, short, broad lungs with narrow upper lobes, and a digestive system high in the abdomen and of quite marked tonus. The stomach is small, steer-horned in form, and transversely placed. Gastric peristalsis and motility are rapid and the stomach emptied in three to three and one-half hours. It is characterized as hypertonic. The small intestine does not rest in the pelvic basin, the cecum is high in the right iliac fossa and the colic flexures are high, particularly the splenic flexure, which is often on a level with the fundus of the stomach. The transverse colon is on a level with the umbilicus and presents haustra which are small and numerous. The sigmoid flexure is short. Barium meal residue, twenty-four hours after ingestion, is either small or entirely absent.

At the opposite extreme, the asthenic habitus is described as of frail and slender build with long, narrow, flat chest, relatively wide pelvis, and narrow intercostal angle. By x-ray the heart is vertical, the lung shadows are long, narrower at the base, and broader at the apices. The greater curvature of the stomach rests in the true pelvis, and the small intestines are in the true pelvis. The colon is low and usually spastic, although sometimes atonic, and presents haustra which are few and large. The stomach empties in six hours and is described as atonic. There is usually considerable twenty-four hour barium residue in the colon. The two intermediary stages are gradations between these extremes. The sthenic habitus is characterized radiographically by the orthotonic type of stomach which may be tubular, bulbous or fish-hook in shape and which empties itself as a rule within three and a half or four and a half hours. Hyposthenic individuals present general physical characteristics approaching more nearly the asthenic type. In them the stomach is hypotonic, fish-hook in shape, the lesser curvature lies below the interiliac crest and the pylorus is at the umbilicus. Peristalsis and motility are poor and the stomach usually does not empty itself in less than five or six hours. The small intestine is a pelvic organ and the cecum is low and towards the midline.

Ansell emphasizes the statement that only the asthenic type is usually considered as needing remedial therapy, whereas frequently the hyposthenic needs it as badly. Even a few with sthenic habitus are improved by similar treatment. He also calls attention to the fact that at times the stomach may be in good position and of good tonus, but the colon markedly prolapsed. This would

illustrate the importance of always making a complete roentgen examination. He also touches on the differential diagnosis from ulcer, appendiceal and gall bladder inflammation.

Concerning treatment a few words may be said. Various procedures are recommended from physical exercise at one end to pure mental therapy at the other. The former seeks two results,—first, by exercise and a more evenly balanced daily routine to alleviate the constipation and, second, to strengthen the abdominal and thoracic musculature. The theory concerning the latter is that with more powerful chest muscles and better physical carriage the intercostal angle becomes widened. This increased flaring of the lower rib margins with the resulting increase in size of the upper abdominal aperture will result in a raising of the various abdominal organs from their prolapsed position. The ligaments are not shortened, but their upper attachments are raised and spread apart. The mechanism may be likened to the raising of the sliding cylinder on an umbrella stick, the steel supports representing the ligaments, and the umbrella when closed corresponding to a narrow intercostal angle, or when opened to a wide angle. However, it is uncertain to what extent muscle training can alter skeletal conformation.

Psychotherapy alone in certain cases undoubtedly does good. This type of individual is usually rather nervous and at times markedly so. Food of proper quality and character, sufficient healthy exercise of any sort, and ample opportunity for mental employment are the three essential conditions of therapy, to which should be added additional details strictly according to the exigencies of the individual case. Perhaps no two cases will be treated in the same manner. The fundamental process is quite similar in all, but the individual reaction is different. These reactions must be studied and treated accordingly. As a rule drugs are to be avoided, although at the beginning of the treatment, when it is highly important that the physician gain the complete confidence of the patient, their use is at times justified. At other times much better results are obtained by avoiding all drugs from the start. Often a patient who has been for years on a very closely restricted diet, when placed immediately on a large and varied diet, will after considerable misgivings discover that it is true that he can eat practically whatever he pleases. McClure reports very satisfactory results with this method.

In short, after ruling out other organic disease and after applying the basic principles enumerated, each case must be treated according to its own merits.

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—*W. T. V.*

Army Base Hospitals to be Held Intact

IN accordance with the wishes of the military authorities and as part of the peace program of the American Red Cross, Base Hospitals organized by the Red Cross for the Army, and which saw war service, will be held intact against future emergencies. War may never again visit this country, it is true, but there are the great disasters of peace—floods, earthquakes, epidemics—which might require immediate facilities, such as only could be supplied by a carefully organized and equipped system of base hospitals, which the Red Cross has as a legacy from its war experience.

These fifty base hospitals are located at important points through the country and their personnel recruited from the staffs of the hospitals in their vicinity. As a result of their war service, the doctors and nurses are incomparably well fitted to undertake such emergency tasks, and virtually, in all cases are being kept enrolled for duty when needed.

The army is cooperating with the Red Cross by providing each base hospital with a unit of equipment in accordance with military standards, stored in a government storehouse as near as possible to the city in which the base hospital is situated. Red Cross Chapters, also, are assisting in the reorganization of the base hospitals for peace times, and will cooperate when base hospitals may be called for emergency service.

A Caucasian Medical School

THE gift of supplies and equipment for the new City Hospital at Ekaterinodar, in southern Russia, by the American Red Cross, has served as a stimulus to the establishment of a first class medical school in the Caucasus.

The hospital, which occupies the former "gymnasium," or high school building, is complete with wards containing 350 beds, laboratories and three operating rooms, and is one of the most modern buildings in the country. It covers a ground area of about five acres, is constructed of red brick and sandstone, and faces the park of the Cathedral. To the right of the main entrance is a bronze tablet, inscribed: "This Hospital Was Established Through the Generosity of the People of the United States of America by the American Red Cross, 1919."

The equipping of the hospital was effected with medicines, instruments and supplies landed from a Red Cross ship at Novorossick, which were installed under the direction of Dr. J. J. Szymanski of Passaic, N. J.

The staff has some of the best professors and surgeons of Petrograd and Moscow, who fled to the Cossack State at the beginning of the Bolshevist regime. Professor Alexiensky, formerly of the University of Moscow, will be chief surgeon. The school will therefore have the benefit of some of the finest medical and surgical talent in Russia.